




CardioNutrition #3: Critique of "Effects of n3 Fatty Acid Supplements in Diabetes Mellitus: ASCEND Study" *New England Journal of Medicine* 2018 Aug



CARDIONUTRITION #3: CRITIQUE OF "EFFECTS OF N-3 FATTY ACID SUPPLEMENTS IN DIABETES MELLITUS: ASCEND STUDY" *NEW ENGLAND JOURNAL OF MEDICINE* 2018 AUG



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- Major books include *Inflammation Mastery 4th Edition* (and any later versions) printed also in separate and progressive volumes as *Textbook of Clinical Nutrition and Functional Medicine* (2016), with excerpts published as *Brain Inflammation* (2016), *Human Microbiome and Dysbiosis in Clinical Disease* (2015); anticipated new books include *Deciphering the Gut-Brain Axis in Clinical Practice* (2018) from which *Autism, Dysbiosis, and the Gut-Brain Axis* (2017) has been prereleased.
- Peer-reviewed/independent publications include: *TheLancet.com*, *British Medical Journal* (BMJ), *Annals of Pharmacotherapy*, *Nutritional Perspectives*, *Journal of Manipulative and Physiological Therapeutics* (JMPT), *Journal of the American Medical Association* (JAMA), *Original Internist*, *Integrative Medicine*, *Holistic Primary Care*, *Alternative Therapies in Health and Medicine*, *Journal of the American Osteopathic Association* (JAOA), *Dynamic Chiropractic*, *Journal of Clinical Endocrinology and Metabolism*, *Current Asthma and Allergy Reports*, *Complementary Therapies in Clinical Practice*, *Nature Reviews Rheumatology*, *Annals of the New York Academy of Sciences*, and *Arthritis & Rheumatism*, the Official Journal of the American College of Rheumatology.

The video of this presentation is archived at ichnfm.org/18, and the transcript in PDF format—which is considered the final and citable version—is archived at academia.edu/37326521; any corrections or updates will be made to the PDF file. The video contains citations which are not replicated in the PDF document; both the video and the PDF transcript should be reviewed for a complete representation of the information. This version was updated on **September 2, 2018**.


Introduction: Good morning, everyone. This is Dr. Alex Vasquez, and today I have a new review for you. I'm going to call this "Cardionutrition #3" since it combines the topics of cardiology, preventive medicine, and of course nutrition. This is going to be a critique of the recently published article "Effects of Omega-3 Fatty Acid Supplements in Diabetes Mellitus" also described as the "ASCEND study." This was recently published in the *New England Journal of Medicine* 2018 in August.

Structure...or not: So as usual, let's begin by taking a look at the structure and the details of this article. This is a randomized trial involving more than 15,000 subjects. This was started in 2005, and that date is important, and I'll point that out as we go through the details here. The intervention here was one capsule per day. Some people also received aspirin, but the authors did not discuss the details. And one of the interesting characteristics of this article ... I'm going to show you some unique characteristics as we go through ... but one of them that I want to point out right now is the lack of detail. So, for example, they barely mentioned that some of the patients received aspirin, but they didn't describe within the study structure who received aspirin, and what the adverse effects were, and what the consequences were, and how were patients selected to receive aspirin or not receive aspirin. They just said some patients received aspirin. But without a description, first of all, that tells us nothing as the reader. That doesn't tell us what's going on within the study. And second of all, a characteristic of valid research is that it can be tested by an independent researcher and replicated; another researcher should be able to read this study and try to replicate it to see if these findings are valid. But when the details in the structure of the research is very vague,

another researcher couldn't follow the study up and do the same procedure, because the procedure isn't described adequately within the study. I am going to point out, because it was notable in this study ... and I don't see this very often ... but what I did see in this study is they had basically some gaping holes in their description of the study methodology and a few other gaping holes that are perhaps at least as bad if not worse.

Structure...revisited: So again, within the structure of this article, subjects received either one capsule per day of fish oil, which provided 840 milligrams of EPA and DHA. If you have followed my work, and if you've looked at my other publications and my recent video on this topic, then you know that **840 mg of EPA and DHA is less than half of the recommended dose for cardiovascular disease prevention**, especially for high-risk patients. So again, this is less than one half of the recommended dose. I invite you to take a look at my other video produced earlier this year. The other subjects received a quote/unquote "placebo," but it wasn't a placebo. It was olive oil arguably ... well, it's not even arguable: **olive oil is one of the most cardio-protective foodstuffs available through diet or supplementation, and so calling olive oil a placebo completely invalidates this entire study**. We could stop the review right here and say, "Okay, the study is bogus." Of course, we can look at their findings; we can see if we can learn something from it. But in terms of comparing fish oil to a placebo to assess the validity of using fish oil as a treatment for the prevention of cardiovascular disease, this study is completely invalid.

Now again, we can look at it to see if we can learn something, but in terms of learning whether or not fish oil is effective for cardiovascular disease prevention, we're probably not going to find it in this study, because their study design was flawed from the very beginning. And in my opinion, that could not have been an accident. **When they started this study in 2005, they clearly had access to information showing that olive oil was cardioprotective**. So, they bungled their own study. The study is a completely mistake. It was a waste of their time. It's a waste of the publication. And yet, this study is going to be used, even now in 2018, to discredit nutritional supplementation. And that's where the real scientific crime occurs here. This study should not have been conducted from the start. It should not have been published, and it shouldn't be praised or used as a citation as if it were providing us with valid information, because it's not.

<p>DR VASQUEZ'S RESEARCH REVIEW</p> <p>Today's main article being reviewed</p> <p>Problems with this publication</p> <p>Noting the pattern of bogus research</p> <p>What can be done</p> <p>What clinicians should do</p> <p>Critique of "Effects of n-3 Fatty Acid Supplements in Diabetes Mellitus: ASCEND Study" New England Journal of Medicine 2018 Aug</p>	<p><u>Olive oil is not a placebo but is clinically active in humans, starting with low doses: biological mechanisms</u></p> <p>▶ Mechanisms of action and biological plausibility: Squalene is also worthy of consideration</p> <p>▶ Oleic acid: May be described as a "conditionally essential nutrient"; component of cell membranes and thus modifies inflammatory mediator production and transmembrane signaling; directly cardiovascular-protective; "interferes directly with the inflammatory response that characterizes early atherogenesis... decreases the expression of several endothelial leukocyte adhesion molecules, among which vascular cell adhesion molecule-1, involved in the selective monocyte recruitment in the arterial intima. Oleic acid also determines a parallel reduction in messenger RNA for this molecule, interfering with the activation of the most important transcription factor controlling endothelial activation, nuclear factor-kappa B. ... oleic acid may contribute to the prevention of atherosclerosis also through a modulation of gene expression for endothelial leukocyte adhesion molecules" per Massaro et al, <i>Cardiologia</i> 1999 Jun</p> <p>▶ Phytochemicals/polyphenols: Ibuprofen-like antiinflammatory activity; notably potent antioxidant and antiinflammatory activity; "antidiabetic effect" per reduction of glycosylated proteins such as HgbA1c and normalization of fasting glucose even at low doses; inhibition of HER2 (erbB-2)-induced malignant transformation (breast cancer); neuroprotective; modulation of gut microbiota is notably relevant for T2DM.</p> <p>For additional context, clinical applications, and disease-specific as well as general protocols, see Inflammation Mastery 4th Edition ichnfm.org/im4 and/or the two-volume set Textbook of Human Nutrition and Functional Medicine from amazon.com/author/alexvasquez</p>	<p>ALEX VASQUEZ DO ND DC FACN</p>  <p>Doctor of Osteopathic Medicine (DO—UNTHSC, USA) Doctor of Naturopathic Medicine (ND—Bastyr University, USA) Doctor of Chiropractic (DC—Western States, USA) Overseas Fellow, Royal Society of Medicine Fellow, American College of Nutrition Author of Inflammation Mastery, ICHNFM.ORG/im4</p>
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So again, olive oil is quite obviously one of the most potent cardioprotective and antiinflammatory foodstuffs available. It is not a placebo, especially for the prevention of cardiovascular disease. And its use as a comparator invalidates the findings of this study; I'm very clear on that. Data suggesting health benefit of olive oil, especially a cardio-protective benefit, was available from the original Keys study back in 1966, and this was recently reviewed

in the *New England Journal of Medicine* in 2003, which was obviously two years before they even started this study. So, the *Journal* could have used its own citation to refute this study, which it then later published 15 years later. And that's just ridiculous. So, in 2003, Hu published a brief commentary editorial titled "Mediterranean Diet and Mortality, Olive Oil and Beyond", in which he discussed the Keys study, which was started back in the 1950s? And again, they knew that olive oil was cardioprotective. Therefore, it has no place being described as a placebo. That's an intellectual error by itself, let alone using it within a study and then publishing that study as if it were to say something. It doesn't say anything other the fact that these people are either intentionally ignorant or just completely clueless.

"The concept of the Mediterranean diet originated from the Seven Countries Study initiated by Ancel Keys in the 1950s. The study showed that, despite a high fat intake, the population of the island of Crete in Greece had **very low rates of coronary heart disease and certain types of cancer and had a long life expectancy**. The traditional dietary patterns typical of Crete, much of the rest of Greece, and southern Italy in the early 1960s were considered to be largely responsible for the good health observed in these regions. **The main characteristics of the Mediterranean diet** include an abundance of plant food (fruits, vegetables, whole-grain cereals, nuts, and legumes); **olive oil as the principal source of fat**..." Hu FB. The Mediterranean diet and mortality—olive oil and beyond. *N Engl J Med*. 2003 Jun 26;348(26):2595-6

By 1986, the entire cardiology, nutrition, and epidemiology world were aware that olive oil was cardio-protective. So, first of all, again, describing olive oil as a placebo for anything is a lie, because olive oil is very biologically active, and the clinical trials have proven that now for decades. Olive oil can never be used as a placebo in any study. At the very least, we have to call this **intentional ignorance**. I would probably describe it also as strategic ignorance, or a **strategic feigned ignorance**. They're trying to pretend that they're ignorant, but they're doing so in a strategic manner. And I'll be very clear on what I think that strategic manner is. If you want to be *mild* about it, you can say *intentional ignorance*. If you want to be a little more clear, in my opinion, you could use a term by Professor Henry Giroux called *The Violence of Organized Forgetting*. Is bad research a form of violence against people? Well, what is violence? Violence is that which hurts people intentionally, right? So, if we are hurting people intentionally by publishing bogus research, is that research therefore a form of violence? I think that's an argument that could be made. Whether we call it *intentional ignorance* or the *violence of organized forgetting*, I'll leave that to you and move on in this review.

So, what really happened in this study? Reasonably, we can summarize that both groups received a low or modest dose of cardio-protective intervention. And again, the study is notable for its missing information. **Neither of the two treatments were independently tested for their components**, and both of the treatments ... that is, the active fish oil and the so-called ... well, I'm not going to describe it as a placebo anymore—I'm just going to say it's olive oil. So, they compared fish oil to olive oil, basically. And **then when those treatments were more or less equivalent in their effects, they stated that fish oil is ineffective for cardioprotection**. **But what's actually true, what's actually more accurate to state, is that fish oil and olive oil are both cardioprotective, and the difference using a low-dose intervention like this, which is almost clinically worthless, is that they didn't find a significant difference between those two interventions, both of which, again, are biologic and cardioprotective.**

Let's look at some of the details now. So, the drug company, Mylan, had paid at least 19 of the authors, oversaw the study design, and supervised its paid consultants at key meetings. And this is within the study description; I'm not making any of this up. I'll show you the actual documents here in just a moment. So, we have a drug company paying the authors of the study. We have a drug company supervising the study research meetings and their paid consultants. The drug company provided the treatment and both the fish oil and the olive oil, neither of which were independently tested for their components, which is also suspicious. And I'll explain to you why I'm even more suspicious. And this drug company also makes the main competing drug in this category, which is a statin drug called simvastatin.

Looking at the article: So here, we're actually going to take a look at the article itself. I'm not going to spend a lot of time on this, and obviously I'm not going to read it word-for-word. But let's at least go through some of the information. So again, "Effects of omega-3 fatty acid supplements in diabetes mellitus"; this is the so-called ASCEND study, a big collaborative group, as if that sounds important. This article was just published August 26, 2018. They've got more than 15,000 subjects. They either received fish oil or olive oil. Again, olive oil should never

be described as a placebo. That's just ridiculous. Medically and biologically, that's a ridiculous statement, and it's just a lie. It's just not accurate. Again, some of the patients got aspirin, but that was very vaguely described. So again, olive oil is clearly not a placebo, since it's antiinflammatory and cardio-protective just as are the omega-3 fatty acids, EPA and DHA.

So, this was published out of the University of Oxford, which interestingly enough also published the other fatty acid study this year, Associations of Omega-3 Fatty Acid Supplement Use with Cardiovascular Disease Risks. I reviewed this earlier this year. This was also published out of Oxford, and this article is a complete disaster, a complete embarrassment to the field of cardiology and the journal, *JAMA Cardiology*, and clearly an embarrassment to the University of Oxford that they would allow this to be published under their name. University of Oxford apparently provided some staffing and structure for the publication of this article. Now look at where we go from there. The trial was funded by the British Heart Foundation, so that sounds great. **Look, we've got a study coming out of the University of Oxford. It was funded by the British Heart Foundation. That sounds so great. It sounds so academic and so clean** until we actually look at the details.

The corporate connections: Capsules containing the omega-3 fatty acids and matching placebo were provided by the drug company Mylan, which makes simvastatin, which is the competing drug and probably in the medical world considered one of the drugs of choice for cardiovascular disease treatment and prevention. Another drug company, of course, Bayer, provided the aspirin and placebo. So, before we go on, I just want to point out ... and you can make a mental note of this ... let's look at the drug companies Mylan, Bayer, and also Solvay and Abbott.

According to the text of the article, "Mylan, Solvay and Abbott had nonvoting representation at meetings of the steering committee of the study and provided comments regarding the trial design and draft manuscript." That's among the most bizarre statements I've ever read in my more than 20 years of looking at research. So again, in more than 20 years of looking at research, I've never seen a study that had a drug company **provide the products that were being studied**, also **paying most of the authors of the study**, and also **being allowed to attend the structural meetings of the study design**. That's, again, something that occurs to me as among the most bizarre things I've ever read in more than 20 years of looking at biomedicine, **that they would have a drug company so well embedded and infiltrated into the study design**, providing the placebo, providing the active treatment, and attending the meetings, and paying many of the authors. That's just exceptional. So, let's continue taking a look at this.

Again, look at what they state here, that this is coming out of "University of Oxford" and the "British Heart Foundation." You also notice among their affiliations, **they don't mention anything about affiliations with drug companies**. They do mention a little bit of Oxford here. But typically, conflicts of interest are published either on the first page or at the end of the article; let's see if they followed that routine here. Some of the patients were already taking fish oil, *and they were allowed to continue taking fish oil on top of the treatments in the study*. So again, that's fishy, if I may say so; that's obviously a pun. I think we'd all agree that this is a bit fishy that they were allowed to take their own independent fish oil supplements in a study supposedly comparing olive oil to fish oil. So that certainly compromises their design.

The trial design should be described clearly within the text of the article: Let's look here at what I mentioned previously. Placebo aspirin in a separate portion of the trial, but they didn't mention what that is. What is the separate portion of a trial? Who received aspirin, etc.? I was a bit perplexed by that. And I have the right to be confused by this article, because this article is confusing. If they don't describe clearly how they conducted the study, then the fault is theirs. The fault is not mine. If I'm reading this, and something doesn't make sense, then it's because they perhaps didn't want it to make sense. But this doesn't make sense to me. I've read this article twice, and I don't see where they described that at all. Eligible patients, again, received 840 mg of EPA and DHA or olive oil. And some people received aspirin, but that was not described. Well, it's a little bit confusing. I'm not too concerned about 100 mg of aspirin, but when we're looking at a large study that's looking for small changes and small details, then every detail matters. So perhaps this is relevant. Or what was the placebo? So, they gave a placebo without describing what the placebo is. Well, what's the placebo? The pill has to be made out of something. Was it magnesium? Was it lactose? Was it potassium citrate? What was it? What was in this pill that may have affected the results? Again, that data is mysteriously missing.

So again, they started this in 2005, as I mentioned previously. The use of over-the-counter fish oil supplement was reported by 10% of patients at baseline, and then some of them had discontinued by the end of some of the follow-up...but not all of the follow-up. So again, that was a bit suspicious. And my question here as I was reading this is, obviously, **where is the data?** So, they've got 10% of their patients taking a fish oil supplement on top of the olive oil or fish oil that they're using in the study. And we have no idea what's going on with the aspirin, because they didn't include the data. So, my question is where's the data?

Unusually high baseline omega-3 index and unusually high response to treatment: They did look at the omega-3 index in 152 patients. 152 patients out of 15,000 is 1%, actually less than 1% of the patients. So, I don't really know what they can state based on looking at 1% of their population. Also, let's take a look at this. Little change in the percentage among patients in the olive oil group. So, this is consistent with what we would expect mostly. And what I mean to point out is the fact that their omega-3 index actually reduced a little bit in the olive oil group. We would expect that, because the oleic acid would displace some of the EPA and DHA while also providing its own cardio-protective benefits. **The world does not revolve around the omega-3 index. Other constituents such as oleic acid and especially the polyphenols within olive oil also provide cardio-protective benefit independent of the patient's decreasing or increasing omega-3 index.** So, this is exactly what we would expect.

Now you'll notice, again, **in the olive oil group, they started at an omega-3 index of 6.6. that's actually a little bit higher than what we would expect.** The typical omega-3 index in an untreated population, just your typical population, is actually in the 5s, not in the 6s. So, this is actually slightly higher than we might expect. But **in the fish oil group, they started at an omega-3 index of 7.1—that's notably higher than average.** The fact that **they went from 7.1 to 9.1 on a low-dose fish oil supplement is also a little bit suspect** in the sense that it's out of normal. The fact that they were impressively different from the olive oil group is one thing that I'd like to point out. The olive oil group started out a little bit better than average, and the omega-3 group was definitely better than average. And then **their change from 7.1 to 9.1 is actually remarkable for such a low-dose supplement.** So that whole thing looked a little suspicious to me, and that's exactly why **in a study like this what should have been done is independent laboratory analysis of both the active treatment fish oil and also in this case the other group's treatment, which was the olive oil.** Somebody should've looked at that independently to see why this change occurred so impressively.

So **typically to achieve this level of change would require about 1900 mg, or almost 2 g per day of EPA and DHA.** And these patients were receiving less than half of that, and I was pretty impressed by that change. I'm just curious as to how that happened. And again, they did not provide independent analysis. So, my note here in the margin ... **this is far above the typical values in terms of baseline and response with regard to the omega-3 fatty acid index.** And again, they only looked at that in less than 1% of their subjects, so I can't state that that's a really good methodology.

We also note that about half of the patients were *obese*, and 94% of them were diabetic. Also 75% of them were *already on a statin*. So why isn't any of that mentioned in the title of the article? If we're looking at omega-3 fatty acid supplements in diabetes, we're not simply looking at diabetes. We're also looking at diabetes with obesity and a lot of patients treated already with a statin. So why isn't that mentioned in the title when it was so clearly obvious in their patient selection? I was a little bit curious about that as well.

Oh, let's take a look at this. We're going to start looking at these charts here. Sometimes these are called forest plots. Notice that the clinical responses to n3 fatty acids were actually better than olive oil in terms of preventing first cardiovascular events. We definitely see priority here for omega-3 fatty acids. If we look here, things are looking pretty even. But again, it doesn't mean a lot when we're comparing omega-3 fatty acids with olive oil. **Who's to say that one would be better than the other at this low dose when both are already known to be cardioprotective?**

"Discussion: Patients with diabetes and no evidence of cardiovascular disease received daily regimen of omega-3 fatty acids, low dose, or low-dose olive oil and did not have a significantly lower incidence of serious vascular events than those who received the [olive oil]." So again, what they're trying to state here is that fish oil provided no benefit. Again, they studied the fish oil against an active treatment, so it's not really a placebo-controlled study. This is a comparative study. Again, we see some benefit here of the low-dose fish oil. It was low

dose but obviously not low potency, because they received a tremendous increase in their omega-3 fatty acids index from what was otherwise described as a low dose. I suspect that their product was inappropriately labeled.

"In conclusion, among patients with diabetes but without evidence of cardiovascular disease at baseline, no significant difference among vascular events between fatty acids and [olive oil]." Again, their use of the term placebo is completely inaccurate. It's linguistically or grammatically inaccurate, and therefore, of course, even worse, it's scientifically and medically inaccurate. This is the inaccurate and inappropriate use of language here. This is not a placebo; the use of olive oil is *indeed* active treatment.

Bayer provided the aspirin and placebo, which were not otherwise described. And the drug company, Solvay Abbott and Mylan, provided the omega-3 fatty acids and the olive oil. So impressive is the observation that those were not independently analyzed. That would've been much more legitimate instead of just taking these products from the drug company that has a vested interest in this study and then saying that everything was okay. They don't know.

And you'll notice that we're at the end of the article here. "Affiliations of the members of the writing committee are as follows..." The list academics, academics, academics, college, college, Cambridge, Leeds General Infirmary, University Hospital, all in the U.K. So where are the other affiliations? You'll notice ... and again, like I said, this is the end of the article. This is the final page. We see no information at all in this article about disclosures, affiliations with drug companies, anything like that. We just don't see it. It's not in this article. It's not on the first page, it should've been here on the first page. At the very least, it should've been here at the end of the article. **They mentioned affiliations here, but why don't they mention all of the affiliations? This is very selective information here.** So again, this article just made me very suspicious.

"Supported by grants to the University of Oxford from the British Heart Foundation." "University of Oxford" again. "Strategic partnership...strategic partnership." Yeah, *strategic*. That's probably worth underlining. British Heart Foundation, etc. So, let's look at that strategic partnership. Let's go look at the data on their conflicts of interest. **So why wasn't this information included in the published study as it was? If we go to the *New England Journal of Medicine* website, then we get to access these disclosure forms.** And look at what we find when we access these forms. We find that the authors are paid by:

1. Medical Research Council U.K.
2. Cancer Research U.K.
3. British Heart Foundation
4. **Bayer...**
5. **Bayer...**
6. **Bayer...**
7. **Bayer Pharmaceuticals** *again*
8. **Solvay Pharmaceuticals**
9. **Abbott Pharmaceuticals**
10. **Mylan Pharmaceuticals**

Well, that becomes more interesting. Let's see who else ... Pfizer and Merck. And here again, British Heart Foundation, Bayer Pharmaceuticals, Bayer Pharmaceuticals, Bayer Pharmaceuticals, Bayer Pharmaceuticals, Solvay Abbott, and Mylan again. Mylan again is the company that makes simvastatin, as you can see from their product description page and also the label for the bottle.

What is this drug used for? It's used in patients at high risk for cardiovascular disease with or without existing coronary heart disease. The goal of this drug is to reduce the risk of total mortality by reducing cardiovascular coronary heart disease deaths, major vascular events, major coronary events, stroke, etc.

So obviously this drug company, Mylan, has a commercial interest in this multi-million, multi-billion-dollar drug called simvastatin. And what do you know? They're actually funding many of the researchers who participated in this study. And again, the structure of the article should've disclosed this, and it wasn't disclosed. In this case, I had to go to the *New England Journal of Medicine* website and look up the information. Again, Bayer Pharmaceuticals, Bayer Pharmaceuticals, Bayer Pharmaceuticals, Bayer Pharmaceuticals, Solvay Abbott, and Mylan.

What my point is in repeating this information is to get you to see the pattern here. What you're going to see here is a pattern that all of these researchers who disclosed financial arrangements with drug companies, they

all have the exact same pattern of financial agreements. Medical Research Council, Cancer Research U.K., British Heart Foundation, Bayer, Bayer, Bayer, Solvay Abbott, Mylan. So that's the third at least time that we've seen this pattern. Now we're looking here again. Exact same pattern. Bayer, Solvay Abbott, Mylan. Let's look at it again here. Bayer, Solvay Abbott, Mylan.

So are we supposed to assume ... first of all, the data wasn't provided in the article. And then when we look at the data, as we are looking at it right here, are we to assume that this was just random chance that all of these authors who were paid by drug companies happen to have been paid by the exact same pattern of pharmaceutical interests? That's an impressive coincidence.

So again, Bayer, Solvay Abbott, Mylan. No wonder they didn't want to publish this. Bayer, Solvay Abbott, Mylan. Bayer again, Solvay Abbott, Mylan. How is it that all of these authors who disclosed payments from drug companies have the **exact same pattern of payment** for this article, and again, this drug company Mylan provided the active treatment as well as the comparator treatment and was present at the meetings for the structure of the study. I've just never seen anything like that. And here we are again. You'll notice I highlighted when I saw conflicts of interest here, and I basically had to highlight the whole section here. And again, it's the **exact same pattern every time**. British Heart Foundation, Bayer four times, Solvay Abbott, Mylan. That's quite impressive.

Here we are again. Exact same pattern of funding for each of these authors. Bayer, Solvay Abbott, Mylan. I've never seen anything like that. They don't have much variation or variety in their study designers or their authors. They seem to be cut all from the same cloth. Bayer, Solvay Abbott, Mylan. That's pretty impressive. That can't happen by chance. This can't be random. Bayer, Solvay Abbott, Mylan. *Sorry, I don't mean to skip anyone*. Again, Bayer, Solvay Abbott, Mylan. The exact same funding pattern for each one of these researchers. I've just never seen anything like that in more than 20 years of looking at research. This article is among the most curious I've ever seen.

Same pattern previously. Same pattern again. So that's impressive. This should've been reported within the printed article on the first page. It wasn't. It should've then been printed at the end. **They provided academic and non-profit affiliations on the first page, but they didn't provide any drug company affiliations.** And then at the end of the article, they provided other affiliations. But again, **they intentionally excluded any mention of author payment by these drug companies.**

Returning now back to my slide presentation, let's just look at those four last points. The drug company Mylan paid at least 19 of the authors, oversaw the study design, and supervised its paid consultants at key meetings of the study, provided the treatment and the comparator substance which was not independently tested to their convenience of course, and makes the main competing drug which is simvastatin. So that's very curious.

Listing of problems: Now let's look at my very brief list of problems with this article. So, we looked at the study design and the population, a randomized trial of 15,000 subjects with diabetes, also obese, also most of them taking a statin drug. This was started in 2005.

1. **Olive oil is biologically active, antiinflammatory, and cardioprotective starting at low-doses and is cannot be described as "placebo" in a cardiovascular and mortality study:** The use of olive oil as the inactive treatment is absurd and invalidates the placebo-controlled claim of the study, given that olive oil is well known ... it's well known now, and it was well known then ... to have antiinflammatory and cardio-protective benefits and has indeed been proposed to be one of the most health-promoting and heart-protecting dietary components available. This was published as early as the 1960s. Certainly by 1986, it was well known. And it was actually reviewed in a *New England Journal of Medicine* in 2003, which was two years prior to the start of this study, which was then later published in the *New England Journal of Medicine* 15 years later. This major error alone is sufficient to invalidate the conclusions of this study. So again, we don't have to go any farther than this. We could stop here and say, "Okay, this research is not worth looking at." But since I went ahead and read it anyway, let's look at the other problems.
2. **Excessive drug company involvement in leadership meetings:** Why were the drug companies invited to the leadership meetings and the design meetings of this study? In more than 20 years of looking at research, I have never seen anything like this. "Mylan, Solvay and Abbott had non-voting representation at meetings." Well, that's nice that they say that they were not voting, but they were supervising their paid consultants at least 19 of which were paid by these drug companies. "Mylan, Solvay and Abbott had nonvoting", supposedly ... that's kind of ridiculous by itself. Anyway, I'll try to finish this sentence. "Mylan,

Solvay and Abbott had nonvoting representation at meetings of the steering committee and provided comments ... and provided comments regarding the trial design and draft manuscript." That's absolutely insane. While supervising their paid consultants at these meetings. I've never seen anything like that.

3. Excessive drug company involvement in treatment provision: The drug company that makes the competing drug in this class of cardioprotection, which is the statin drugs and specifically in this case, simvastatin ... the drug company that makes a competing drug was allowed to furnish the products. Mylan provided the omega-3 fatty acids and the comparator treatment.
4. Failure to publish drug company payments to authors within the publication: Again, 19 of the authors were paid by the drug companies that have vested interest in this study, and the conflicts were not printed in the article. I've never seen [such a huge conflict of interest] so big and so obvious as to have 19 authors paid by the drug company that has a vested interest in the study, and *none of it was mentioned in the published article*.
5. Unusual response to treatments; treatments not independently tested for contents: Problem number five, the products were not independently tested, and the so-called active treatment here, the omega-3 fatty acids, had clinical and biological effects that were inconsistent with what we see in the other studies. These products should have been tested.
6. Unusual baseline omega-3 index, unusual response to treatment; extremely small population evaluation: They tested the omega-3 index in 152 subjects. That's less than 1% of their study population. This is rather weak, and the results were unusual at baseline. They had a high baseline omega-3 index and a remarkably high increase in the omega-3 index with treatment. So again, I think that those products should have been independently tested. That might give me slightly more faith in this publication in which I have zero faith.

Again, let's look at what I had mentioned previously now. I've reviewed it, but I did point that out here on a different slide. Problem number four, authors were paid by the drug companies, and the conflicts were not printed in the article. You can see that the authors were uniformly paid by the same groups, especially Bayer, four times at least here that we're looking at, Solvay Abbott, and Mylan, which again have a very strong interest.

So here's **one** example and then **another** example, number **three**, number **four**. A **fifth** author paid by the same pattern of drug companies. Very interesting. I've never seen that before. Number **six**, number **seven**, ...number **nine**, number **10**, number **11**, number **12**. And here we are at number **13**, and then number **14**, number **15**, number **16**, number **17**, number **18**, and number **19**. **Nineteen authors paid by the same cluster of drug companies, and no disclosure whatsoever within the printed article**. That is exceptional. Again, I've reviewed that now at least twice.

Problem number two. Why were the drug companies invited to the leadership and design meetings of the study? I've never seen that before. They were supervising their paid consultants. So whether they voted or not, they certainly would've provided some pressure. The drug company that makes the competing drug provided the products for this study. That's a bit bizarre as well. And number four and number five I've already repeated, so I won't go through that again.

What can be done: Moving on now towards the closure of this brief review, what do we do with all of this? I notice a pattern of bogus research. I've provided video and transcript reviews of that information. You can download that from the internet, and you can see the video and download the transcript from various locations. I'll provide you some links so you can access that rather easily:

- Short review of "Supplemental Vitamins and Minerals for CVD Prevention and Treatment" <https://vimeo.com/273402598>
- Perpetuating Nutritional Ignorance among Doctors and Recycling Bad Science at JAMA and AMA <https://vimeo.com/265987272>
- Review of "Associations of Omega-3 Fatty Acid Supplement Use With Cardiovascular Disease Risks" JAMA Cardiology 2018 <https://vimeo.com/255648523>
- Critique of "Effects of n-3 Fatty Acid Supplements in Diabetes Mellitus: ASCEND Study" N Engl J Med 2018 Aug; brief version: <https://vimeo.com/287650812>; complete version: <https://vimeo.com/287266715>

Probably nothing can be done to stop the medical-industrial-news complex, but people can inform themselves and learn how to think for themselves rather than submit to supposedly authoritative sources which are really nothing

more than facades for commercial interests and power structures. Let me go ahead and read that one more time. *What can be done to change the situation of bogus research which influences healthcare policy, insurance coverage, medical practice, and patient care, and ultimately the lives and deaths of millions of people? What can be done to stop or halt or provide some friction to this machine?* Probably nothing is going to stop it. But *what we can do* is try to inform ourselves, learn how to think independently rather than submit to supposedly authoritative sources. I think that's very important. And that applies throughout life, not simply looking at biomedicine. Because these authoratative sources are really nothing more than facades for commercial interests and power structures.

1. Distance: Cancel your subscription to organizations, publications, and companies, and people that lie to you.
2. Nurturance: I encourage you to read real literature, philosophy, and science in order to cultivate a sense of truth. You know, we live in basically a junk culture, and that's true internationally these days. But **if we are surrounded by junk, then we have to make a decided and clear effort to expose ourselves to clarity**. So the solution to junk in our case ... in this case, we're not going to be able to change the entire culture ... but what we can do is **create our own intellectual microenvironments** where we expose ourselves to culture, good writing, good philosophy, good science, good music, and things of a better standard. And in my opinion, that applies throughout life. Music influences thought. Reading influences thought. Videos and audiobooks obviously can influence thought as well. Here are my top three recommendations—listed in descending priority sequence—for life-changing “digital” information; here, I am distinguishing digital from tonal, ie Strunz and Farah, eg, *Primal Magic*:

- 1) [Friedrich Nietzsche: The Giants of Philosophy](#) by Dr Richard Schacht (Author), Charlton Heston (Narrator), ASIN: B000GHMWAI; my advice is to try to **get the audio cassette version** because it is longer and more complete than is the digital version; personal appreciation to Dr Schacht for sending me his original typewritten manuscript
- 2) [Six Pillars of Self-Esteem: The Definitive Work on Self-Esteem by the Leading Pioneer in the Field](#) by Dr Nathaniel Branden; paperback and audiobook ASIN B0000544VI; remarkable for its content as well as the lucidity of its structure
- 3) [Thus spoke Zarathustra](#) (Abridged) by Dr Friedrich Nietzsche. Brilliantly translated, abridged, and performed by Alex Jennings and Jon Cartwright

3. Development: And I also state here the third major bullet point. If you want to be a good thinker, then you have to give time to developing this skill. I'm consistently amazed at how people expect, or they take for granted, the fact that they think they're good thinkers when they've never studied the process. Well, why would that apply to thinking when it doesn't apply to anything else? No one becomes a really great chef or a really great musician without giving some time to practice and study it. I didn't learn *kungfu*, *jujitsu*, and *taekwondo* by sitting on the sofa; I had to go to class and learn how to do those things—and we could all use a million different examples. As an activity, action and skill, thinking is no exception: we have to give time and energy to learn to do it well. If I, or if you, or if we collectively want to be good thinkers, we have to study that process. If you want to understand people, you have to study psychology and sociology. If you want to understand music, you have to give some study to the structure of music. And if you want to understand thinking, you've got to spend some time at least looking at what creates a good argument, what are the logical fallacies that people fall into on a consistent basis, so you can identify those errors in other people's thought and, of course, in your own. In my opinion, the study of psychology and philosophy really helps here a lot, because we grow up in a culture that has a lot of fallacies. And so, if you want to have a good foundation upon which you can then study other subjects like math and science and biomedicine, *et cetera* in my opinion, you're going to be much more effective in those other sciences if you have a strong and clear psycho-social foundation. And that comes from studying philosophy, psychology, sociology, and the history of human thought in order to provided grounding, structure, and perspective.

- The process is not always easy, especially at the start: So, what I did, and I was drawn to do this naturally as a teen basically, but then in my early 20s I certainly dove into this with a lot of energy, and I'm not saying that it was particularly easy. For example, when I first started reading Nietzsche, I didn't understand what he was talking about at all; but I kept forcing myself to read, and eventually now I can read him without any problem. But don't expect it to be easy.

- Change the function and structure of your brain: If you're trying to move from a common level to a higher level of thought, that transition isn't going to be easy and enjoyable all the time. Many times, you'll have to read things that are complicated. You might read the entire chapter for example and not really understand it. You have to go back and read it, and then you maybe read it a third time or something like that, and then finally *it opens itself to you*, or *your mind opens itself to the material*, either way. But don't expect that process to be easy. It's not. You're trying to change the structure of your brain when you take on a new task or a new challenge like that. And so of course your brain is going to have to go through an adaptation process, and that's what we call learning. And sometimes we have to work and struggle to do that.
- This applies to every aspect of your life: *Critical and clean thinking* is a skill that serves you in every aspect of your life, and the reverse is also true. If you're "completely ignorant" with regard to psychology and sociology, then that ignorance and "blindness" and lack of skill are probably affecting your relationships, and that's probably affecting your thought in other areas as well. So, one is not separate from the other. In my opinion, we *need to* or we *can* clarify our emotional lives, psychosocial lives, and then move on to other things such as science.

What clinicians should do: Clinicians should continue using fish oil supplements generally at a dose of 1,900 mg per day if the goal is to optimize the omega-3 index to approximately 10%, and of course, you have to customize that per patient. So, a reasonable dose is a little bit less than 2 g per day of EPA and DHA, and then customize that maybe after about six months or so. You can test the omega-3 index and see where your patient is. Some patients respond a little more quickly than others, while some patients need higher doses; and of course if they're obese or if they have malabsorption, then they will need additional treatment for additional time.

Closure: Thank you very much for your attention during this presentation. This does bring us to a conclusion of this review: "Critique of Omega-3 Fatty Acid Supplements in Diabetes Mellitus, the ASCEND study published in the *New England Journal of Medicine* 2018 August. I think I provided you a competent review. I think this study is absolutely worthless, and it should have not been published. It should be withdrawn. But, of course, it will make the major news internationally because that serves the powerful corporate interests of news, advertising, and pharmaceutical drug sales. ❌

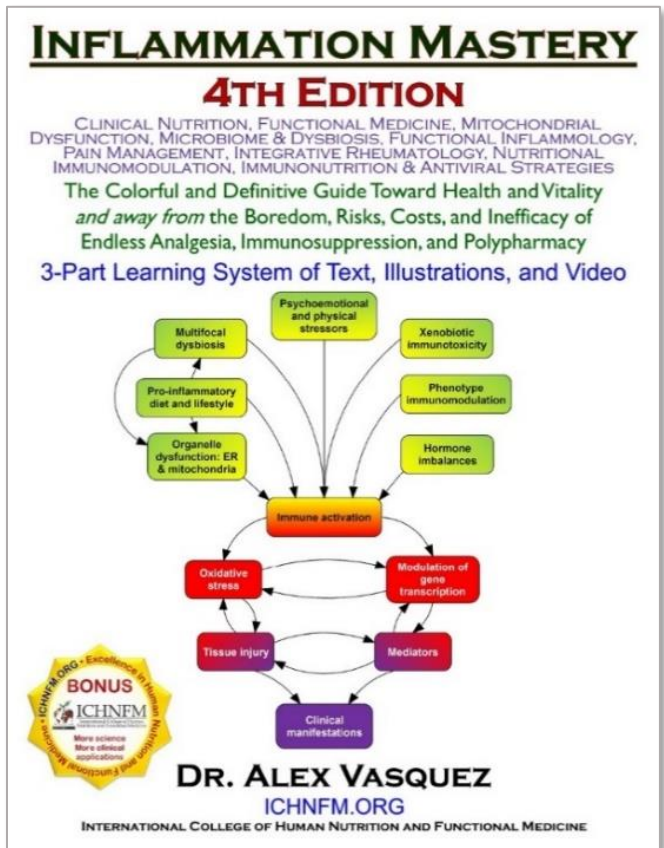
Citation: Vasquez A. Critique of "Effects of n3 Fatty Acid Supplements in Diabetes Mellitus: ASCEND Study" *New England Journal of Medicine* 2018 Aug: Video presentation (ichnfm.org/18) and official transcript (academia.edu/37326521) Date of this revision: September 2, 2018

About the author: Dr Vasquez holds three doctoral degrees and has completed hundreds of hours of post-graduate and continuing education in subjects including Obstetrics, Pediatrics, Basic and Advanced Disaster Life Support, Nutrition and Functional Medicine; while in the final year of medical school, Dr Vasquez completed a Pre-Doctoral Research Fellowship in Complementary and Alternative Medicine Research hosted by the US National Institutes of Health (NIH). Dr Vasquez is the author of many textbooks, including the 1200-page [*Inflammation Mastery, 4th Edition*](#). (2016) also published (by popular student request) as a two-volume set titled [*Textbook of Clinical Nutrition and Functional Medicine*](#). "DrV" has also written approximately 100 letters and articles for professional magazines and medical journals such as *TheLancet.com*, *British Medical Journal* (BMJ), *Annals of Pharmacotherapy*, *Nutritional Perspectives*, *Journal of Manipulative and Physiological Therapeutics* (JMPT), *Journal of the American Medical Association* (JAMA), *Original Internist*, *Integrative Medicine*, *Holistic Primary Care*, *Alternative Therapies in Health and Medicine*, *Journal of the American Osteopathic Association* (JAOA), *Dynamic Chiropractic*, *Journal of Clinical Endocrinology and Metabolism*, *Current Asthma and Allergy Reports*, *Complementary Therapies in Clinical Practice*, *Nature Reviews Rheumatology*, *Annals of the New York Academy of Sciences*, and *Arthritis & Rheumatism*, the Official Journal of the American College of Rheumatology. Dr Vasquez lectures internationally to healthcare professionals and has a consulting practice and service for doctors and patients. Having served on the Review Boards for *Journal of Pain Research*, *Autoimmune Diseases*, *PLOS One*, *Alternative Therapies in Health and Medicine*, *Neuropeptides*, *International Journal of Clinical Medicine*, *Journal of Inflammation Research* (all PubMed/Medline indexed), *Integrated Blood Pressure*

Control, *Journal of Biological Physics and Chemistry*, and *Journal of Naturopathic Medicine* and as the founding Editor of *Naturopathy Digest*, Dr Vasquez is currently the Editor of *International Journal of Human Nutrition and Functional Medicine* and the Director for International Conference on Human Nutrition and Functional Medicine. Dr Vasquez has also served as a consultant researcher and lecturer for Biotics Research Corporation.

Contextualizing resource—same information in different formats and contexts:

- *Inflammation Mastery, 4th Edition* <https://www.amazon.com/dp/B01KMZZLAQ/> and
- *Textbook of Clinical Nutrition and Functional Medicine, vol. 1: Essential Knowledge for Safe Action and Effective Treatment* <https://www.amazon.com/dp/B01JDIOHR6/>



Introductory videos:

- Video introduction to books: <http://www.ichnfm.org/im4> and other videos: <http://www.ichnfm.org/18>
- Conference presentation—introducing the clinical protocol: <http://www.ichnfm.org/video-funct-inflam-1>



See video at <http://www.ichnfm.org/18>

Persistent inadequacies in nutrition education/training among physicians

Introduction: Despite the acknowledged importance of diet in the prevention of obesity, diabetes, hypertension and other components of cardiometabolic syndrome/disease, physicians are consistently and systematically untrained in nutrition. A few exemplary citations are summarized per the following:

- What do resident physicians know about nutrition? (*J Am Coll Nutr* 2008 Apr²⁹): "OBJECTIVE: Despite the increased emphasis on obesity and diet-related diseases, nutrition education remains lacking in many internal medicine training programs. We evaluated the attitudes, self-perceived proficiency, and knowledge related to clinical nutrition among a cohort of internal medicine interns. METHODS: Nutrition attitudes and self-perceived proficiency were measured using previously validated questionnaires. Knowledge was assessed with a multiple-choice quiz. ... RESULTS: Of the 114 participants, 61 (54%) completed the survey. Although 77% agreed that nutrition assessment should be included in routine primary care visits, and 94% agreed that it was their obligation to discuss nutrition with patients, only 14% felt physicians were adequately trained to provide nutrition counseling. ... CONCLUSIONS: Internal medicine interns' perceive nutrition counseling as a priority, but lack the confidence and knowledge to effectively provide adequate nutrition education." These are impressive results showing that internal medicine doctors—specialists who commonly deal with diabetes, hypertension, obesity, and metabolic syndrome—do not have competence in nutrition, even by weak and basic standards.
- Relevance of clinical nutrition education and role models to the practice of medicine (*Eur J Clin Nutr.* 1999 May³⁰): "Yet, despite the prevalence of nutritional disorders in clinical medicine and increasing scientific evidence on the significance of dietary modification to disease prevention, present day practitioners of medicine are typically untrained in the relationship of diet to health and disease."
- How much do gastroenterology fellows know about nutrition? (*J Clin Gastroenterol.* 2009 Jul³¹): "The mean total test score was 50.04%. ...CONCLUSIONS: Gastroenterology fellows think their knowledge of nutrition is suboptimal; objective evaluation of nutrition knowledge in this cohort confirmed this belief. A formal component of nutrition education could be developed in the context of GI fellowship education and continuing medical education as necessary."

In sum: The data consistently demonstrate that healthcare providers at the doctorate level are untrained in nutrition when assessed by rather simple standards; their knowledge of functional nutrition at the level of clinical intervention in the treatment of serious disease would reasonably be expected to be approximately zero. Thus, given that doctors are trained neither in musculoskeletal management (despite the fact that all patients have musculoskeletal systems and that related disorders represent no less than 20% of general practice) nor nutrition (despite the fact that all patients eat food and that such dietary habits (and/or the use of nutritional interventions) impact nearly all known diseases in the known universe), one might wonder as to the cause and perpetuation of this *systematically imposed ignorance* on such topics of major importance. Consistent faults in medical education are not accidental.

Dumbing Us Down: The Hidden Curriculum of Educational Systems

"Look again at the seven lessons of school teaching: confusion, class position, indifference, emotional and intellectual dependency, conditional self-esteem, and surveillance. All of these lessons are prime training for permanent underclasses, people deprived forever of finding the center of their own special genius."

Such a curriculum produces physical, moral, and intellectual paralysis, and no curriculum of content will be sufficient to reverse its hideous effects. ... Schools teach exactly what they are intended to teach and they do it well."

Gatto JT. *Dumbing Us Down: The Hidden Curriculum of Compulsory Schooling*, p. 16

Adverse effects of nonsteroidal anti-inflammatory drugs (NSAIDs), COX-2 inhibitors (coxibs)

Introduction: Nonsteroidal anti-inflammatory drugs (NSAIDs) have many common and serious adverse effects, including the promotion of joint destruction. Paradoxically, these drugs *cause* or *exacerbate* the very symptoms and disease they are supposed to treat: joint pain and destruction. In a tragic exemplification of Orwellian newspeak³²,

²⁹ Vetter et al. What do resident physicians know about nutrition? An evaluation of attitudes, self-perceived proficiency and knowledge. *J Am Coll Nutr.* 2008 Apr;27(2):287-98

³⁰ Halsted CH. The relevance of clinical nutrition education and role models to the practice of medicine. *Eur J Clin Nutr.* 1999 May;53 Suppl 2:S29-34

³¹ Raman M, Violato C, Coderre S. How much do gastroenterology fellows know about nutrition? *J Clin Gastroenterol.* 2009 Jul;43(6):559-64

³² Orwell G. *1984*. Harcourt Brace Jovanovich: 1949. "Newspeak" is defined by the Merriam-Webster Dictionary (m-w.com) as "propagandistic language marked by euphemism, circumlocution, and the inversion of customary meanings" and as "a language designed to diminish the range of thought," in the novel *1984* (1949) by George Orwell.