



# Fish Oil and Elevated Prostate Cancer Risk – Fact or Fiction?

*This article is a rebuttal to the recently publicized negative study of fish oil and prostate cancer compiled by a panel of Nutri-West experts: Lynn Toohey, PhD; Don Bellgrau PhD (NIH grant reviewer); Dan Murphy DC, DABCO (years of research on omega 3's; part time faculty, Life Chiropractic College West); Brandon Lundell, DC, DABCI instructor, Assistant Professor, So. Cal. U of Health Sciences.*

In a word: fiction. Recently, headlines touted a negative association of fish oil and prostate cancer (*Brasky et al. 2013*)<sup>i</sup>, based on an observational study (not a clinical trial proving cause and effect) that analyzed (after the fact) previous data taken from a publication that did not adjust for what they call confounding factors – other factors that can cause prostate cancer. The conclusions that they drew from their observations have been rebutted by experts in the field, and called everything from “silly” to “irresponsible”. An association was not only mistakenly drawn, it was given wide media coverage, mostly because it goes against everything we have been told is true (based on good research) that fish oil is good for us. This misinterpretation of facts certainly does not negate all of the thousands of positive articles on fish oil, which include well-designed, randomized placebo controlled CLINICAL TRIALS, in which participants are actually given fish oil and then results are measured.

**The Science of Interpreting Studies:** It is taught in every first year doctorate program that when you read a study, in order to avoid drawing false conclusions, one must remember the axiom: **Correlation Does Not Imply Causation**. In this study, the flawed correlation of prostate cancer with Omega 3's in the blood does not in any way mean that Omega 3's *cause* prostate cancer. Even if a correlation did exist (which is unlikely as you will see below) the Omega 3's could be elevated because of the cancer and not the other way around. Cancer is known to alter metabolism in various ways, including fatty acid metabolism. It is more conceivable, given the preponderance of evidence of beneficial effects of Omega 3's, that cancer induces inflammatory chemicals which in turn release fatty acids into the blood stream. This could be a host –defense mechanism, or a tactic on part of the cancer cells to supply ample energy for tumorigenesis. In any case, one must remember the axiom “correlation does not imply causation”.

This study in question was riddled with many flaws, including the fact that they did not measure fish oil intake, or even fish oil supplements for that matter (and we all know that there is a difference between farm raised fish and wild caught salmon!) What they measured was the level of fatty acids in the blood for one particular moment in time, a measurement that is known to have wide day-to-day variability. The omega-3 index, which measures both EPA and DHA within red blood cells, is a much more accurate indicator of long-term omega-3 intake and tissue status than is the plasma omega-3 level, which is subject to significant day-to-day variability. They also failed to account for body weight, a factor highly associated with prostate cancer (and more of the prostate cancer group

was overweight). It is suggested that fat cells release inflammatory cytokines, and increased inflammation is a suspected cause of prostate cancer. Many factors contribute to omega 3 blood levels, including other dietary factors, metabolism, genetics etc., and some of the things not taken into consideration included that more than 50% of the prostate cancer group were smokers, consumed alcohol, and were overweight.

Anthony Victor D'Amico, MD, PhD, who specializes in prostate cancer research, notes that while the study adjusted for diabetes and family history, they left out huge factors associated with prostate cancer, such as race, age, PSA level, rectal exam, body mass index, and whether or not they were overweight (already mentioned to be highly correlated). According to Dr. D'Amico, unless you take these things into consideration, "You could associate almost anything with prostate cancer; something like "driving a Cadillac" could be associated with prostate cancer if you don't account for the major factors that cause prostate cancer." Dr. D'Amico also finds it interesting that Table one in the study lists the PSA level and race but those factors were not adjusted for in the model, "maybe because the association was lost once they did."

Even if the blood measurement of fatty acids was a gold standard, which it is not, the clinical relevance of such small differences (.04% EPA and 0.1% DHA) in each of the groups remains unknown. Dr. Don Bellgrau, an NIH grant reviewer, emphasizes that "the assay is quite cumbersome and prone to error, for which they provide no data regarding validation. It involves extracting total lipids from plasma followed by separation of other lipids by chromatography. Most biomarker people would say the more you do to the sample prior to analysis the more likely you are to add error to the process. They also use pooled serum from "healthy volunteers" as an internal control for each assay but do not show any data regarding day to day variability when assaying the same samples. They also express fatty acids as a weight percentage of total phospholipid fatty acids, rather than an absolute value, and using percentages is likely to be misleading."

Dr. Bellgrau further explains how the authors of the article even stated within the article that analyzing in this manner could lead to spurious (false) conclusions. He points out that the authors admit that "because some fatty acids represent greater proportions of the total weight than others"(page 4), they did some **statistical gymnastics** to make the claim that this was a valid approach even though they state later that "spurious associations arise because of measurement of fatty acids as a proportion of total weight rather than absolute concentration" (page 6). This approach is likely what gave them their conclusion (potentially spuriously) because as they state on page 8 "expressing fatty acids as weight proportions could create spurious associations because an increase in the percentage of one type of fatty acid requires a decrease in others". Dr. Bellgrau emphasized that they should have compared by absolute weight, not by percentage.

Another expert who questions the validity of inferring causality from observations that don't take confounding factors into consideration is Michael Savage, PhD. Dr. Savage's PhD is in epidemiology from U of C Berkeley, and he interviews Anthony Victor D'Amico MD, PhD (discussed above) about this "bogus study" reporting "junk science" in the following video:

<http://www.michaelsavage.wnd.com/wp-includes/ms-files.php?file=2013/07/071113-FISH-OIL-INTERVIEW.mp3>

Dr. Savage notes that in addition to not measuring fish intake or supplement intake, there was no consideration for what quality of fish (fresh water fish?) or supplements (molecularly distilled and purified, free of toxins?), the duration of exposure to omega 3's, and whether or not subjects started taking fish oil before or after they were diagnosed with prostate cancer. Given that many people who have heard about the benefits of fish oil would want to supplement with it after a diagnosis, the study

does not consider that the prostate cancer group may have intentionally increased their consumption of omega 3's.

A 2010 study led by the same researcher reported that the use of fish oil supplements was NOT associated with any risk for prostate cancer...

"Although there is evidence from studies of prostate cancer cell lines and rodent models that several supplements may have antiinflammatory, antioxidant, or other anticancer properties, few epidemiologic studies have examined the association between nonvitamin, nonmineral, "specialty" supplement use and prostate cancer risk." They then reported on participants, 50-76 yr, who were 35,239 male members of the VITamins and Lifestyle (VITAL) cohort who were residents of western Washington state, and who completed an extensive baseline questionnaire in 2000-2002. Participants responded about their frequency (days/wk) and duration (yr) of specialty supplement uses. 1,602 incident invasive prostate cancers were obtained from the Surveillance, Epidemiology, and End Results registry. No correlation with fish oil and prostate cancer was observed<sup>ii</sup>.

In fact, a 2010 meta-analysis (analysis of many clinical trials and much much stronger than any "observational" study), "showed a significant 63% reduction in prostate cancer-specific mortality<sup>iii</sup>." Additionally, over 45,000 men were studied by Augustsson K et al., and they found that: "Each additional daily intake of 0.5 g of marine fatty acid from food was associated with a 24% decreased risk of metastatic cancer. We found that men with high consumption of fish had a lower risk of prostate cancer, especially for metastatic cancer. Marine fatty acids may account for part of the effect, but other factors in fish may also play a role."<sup>iv</sup>

Also, it is not a trivial fact that high omega-3 levels are associated with lower rates of death from any cause<sup>v</sup>. Clearly, the benefit of fish oils in the literature remains favorable, and will survive a weak attempt in the mass media to sensationalize a poorly deduced conclusion.

#### References:

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<sup>i</sup> *J Natl Cancer Inst.* 2013 Jul 10. Plasma Phospholipid Fatty Acids and Prostate Cancer Risk in the SELECT Trial. Brasky TM, Darke AK, Song X, Tangen CM, Goodman PJ, Thompson IM, Meyskens FL Jr, Goodman GE, Minasian LM, Parnes HL, Klein EA, Kristal AR.

<sup>ii</sup> *Nutr Cancer.* 2011;63(4):573-82. Specialty supplements and prostate cancer risk in the VITamins and Lifestyle (VITAL) cohort. Brasky TM, Kristal AR, Navarro SL, Lampe JW, Peters U, Patterson RE, White E.

<sup>iii</sup> *Am J Clin Nutr.* 2010 Nov;92(5):1223-33. Fish consumption and prostate cancer risk: a review and meta-analysis. Szymanski KM, Wheeler DC, Mucci LA.

<sup>iv</sup> *Cancer Epidemiol Biomarkers Prev.* 2003 Jan;12(1):64-7. A prospective study of intake of fish and marine fatty acids and prostate cancer. Augustsson K, Michaud DS, Rimm EB, Leitzmann MF, Stampfer MJ, Willett WC, Giovannucci E.

<sup>v</sup> Mozaffarian D, Lemaitre RN, King IB, Song X, Huang H, Sacks FM, Rimm EB, Wang M, Siscovick DS. Plasma Phospholipid Long-Chain omega-3 Fatty Acids and Total and Cause-Specific Mortality in Older Adults: A Cohort Study. *Annals of internal medicine* 2013;158:515-25; Pottala JV, Garg S, Cohen BE, Whooley MA, Harris WS. Blood Eicosapentaenoic and Docosahexaenoic Acids Predict All-Cause Mortality in Patients With Stable Coronary Heart Disease: The Heart and Soul Study. *Circulation Cardiovascular quality and outcomes* 2010;3:406-12.

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*Total Calories 41, Calories from fat 41, Polyunsaturated fat (not less than) 3 grams, Monosaturated fat (not less than) 0.45 grams.*

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