

## Response to Omega-3 / Prostate Risk Study

**Study:** Brasky TM et al. Plasma phospholipid fatty acids and prostate cancer risk in the SELECT Trial. JNCI ePub ahead of print July 10, 2013.

**Background:** The authors of the current study previously analyzed another study, the Prostate Cancer Prevention Trial (PCPT), and reported a link between higher plasma levels of omega-3 fatty acids and higher risk of aggressive prostate cancer.

The same authors sought to replicate their findings in the current study, which analyzed plasma omega-3 levels and risk of prostate cancer in participants of the Selenium and Vitamin E Cancer Prevention Trial (SELECT). The authors again report an association between higher plasma omega-3 levels and increased prostate cancer risk.

**Bottom Line:** The results of this observational study (which do not prove that higher omega-3 plasma levels cause prostate cancer) are in stark contrast to the findings of other studies that do not link omega-3 with increased prostate cancer risk or that show a *protective* effect of omega-3 intake.

Many of the study's findings are contrary to current scientific understanding of prostate cancer risk factors and the mechanisms by which they contribute to risk.

Cancer formation is a long-term process. Plasma omega-3 levels, which were measured as markers of risk in this study, reflect recent rather than long-term intake of omega-3s. Moreover, the differences in plasma levels between men with and without prostate cancer were small.

Taken together, these limitations require that the study findings be interpreted with caution, and that no conclusions be drawn about the omega-3s and prostate cancer.

- This was an observational study, which means that it can only show an association and not a cause and effect relationship between omega-3s and prostate cancer risk. The study's conclusions are also limited by the fact that the SELECT study, whose data was used in this analysis, wasn't designed to evaluate the question the researchers sought to confirm.
- Very importantly, this report conflicts with the findings of many other observational studies that not only demonstrate *no* correlation (association) between omega-3 consumption via fish and/or supplementation and risk prostate cancer risk, but in many cases also showed a *protective* effect against prostate cancer. (References for these studies shown below)
- The authors acknowledge that no mechanism is known that would explain how omega-3 increase prostate cancer risk. In fact, inflammation is believed to play a causal role in many cancers, and the omega-3s possess "anti-inflammatory" actions.

Additionally, in the first study analyzed by these researchers (PCPT), they reported that *high* concentrations of trans-fatty acids (which increase inflammation) were associated with a *lower* risk of high-grade prostate cancer. Thus, neither of these reported associations (for the omega-3 and trans-fatty acids) would be expected and, consequently, raise questions about the findings.

- This study is a prime example of why care needs to be taken in interpreting findings when looking at data from an already published study and trying to make sense of it with statistics:

While the study found a significant correlation or link between omega-3 plasma levels and risk of prostate cancer, it also showed several other significant correlations that don't make sense when viewed against a background of scientific evidence.

The data suggests that *non*-smokers had *more* aggressive prostate cancer. (Smoking has been linked to prostate cancer risk). It also appears that *non*-drinkers, or people who drank less than one alcoholic drink at baseline, were at *higher* risk of prostate cancer. (Alcohol consumption is not considered a risk factor for this cancer). If one were to consume less omega-3 to reduce prostate cancer risk as this study implies, would one also commence smoking and consume more alcohol to decrease their risk?

- While the authors conclude that “the use of nutritional supplements may be harmful”, there is no evidence that anyone in the study took omega-3 (fish oil) supplements. The study didn’t include any information about how omega-3 intake was achieved.

In fact, this study may have simply been measuring a biomarker (plasma levels) reflecting recent intake of fish and/or fish oil supplements in a group of high-risk cancer patients that had been told to increase their EPA and DHA levels, as compared to a group of non-cancer patients that had not been given this advice.

Plasma levels of EPA and DHA reflect very recent intake and are considered a *poor biomarker of long term* omega-3 intake especially when compared to red blood cell levels, which reflect medium-term intake.

A single typical fish oil dose (or hearty serving of fish) results in more than a 100% increase in plasma omega-3 levels. So looking at plasma levels in healthy and sick people may only provide insight into the recent fish consumption habits of these individuals.

- Finally, as pointed out by the industry group Global Organization for EPA and DHA Omega-3 (GOED), the difference in mean plasma omega-3 levels (EPA + DPA + DHA) in the combined prostate cancer groups vs. the control group of men without prostate cancer was tiny —4.66% vs. 4.48% respectively, or about a 0.2% difference. GOED commented that this difference could have occurred by consuming a single serving of fish prior to the blood draw for data collection in SELECT participants.

This small difference in plasma levels linked to the reported large 71% increase in risk should raise a red flag about concluding that higher omega-3 intake raises prostate cancer risk.

## References:

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