

UPDATE

Omega 3 and Prostate Cancer



“Fish and fish oil might be bad for your prostate? Sounds fishy, or more like a whale of a story that baited many folks, but really it is a minnow amongst a gigantic pool of positive research with omega-3 fatty acids.”

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A surprising finding from a single study received almost as much attention as a Congressman from New York that likes to send text messages and pictures to folks he has never met. So, lets review the latest on this controversial study [1] that caused a lot of uproar (aka freaking out), and tell you what I think is really going on here.

Over the last 15 years I have tried to yell from the rooftops that when it comes to lifestyle, dietary supplements and many medications that “Heart Healthy=Prostate Healthy”! “Heart Healthy = Prostate Healthy!” Think about this for a second. Everything and anything over the last several decades that has been effective in reducing the risk of the number 1 cause of death in men and women (cardiovascular disease) has also been shown to either reduce the risk of prostate cancer or the risk of dying from prostate cancer, and most of the major cancers for that matter [2-7]. Reduced calorie diets, fruits and vegetables, fiber, weight loss, exercise, low cholesterol, low blood pressure, low risk of diabetes, not smoking ... you name the heart healthy lifestyle change and it has been found to be prostate healthy. However, cholesterol lowering supplements and medications now have some evidence that they reduce the risk of aggressive prostate cancer or may slow the progression of this disease that we are actually just starting a clinical trial in Canada with Dr. Klotz to see if we can prevent the disease from advancing by using a cholesterol lowering supplement. This clinical trial is also being partially supported by a grant from the PCRI (thanks folks).



“*Whitefish is a low in mercury, very high in omega-3, and tastes GREAT!*”

(Continued on page 4)

And, for the sake of this article and discussion please keep in mind that virtually NOTHING that has been proven to be heart unhealthy from lifestyle changes or supplements has been shown to be prostate healthy. In other words, high cholesterol, high blood pressure, obesity, high blood sugar and insulin, bad diet, and lack of exercise are not good for the heart and not good for the prostate [2-7]. Now, think about your dietary supplements. Selenium and vitamin E in large doses were not found to be heart healthy and now we know that they were not good for the prostate [8]. This evidence of heart healthy=prostate healthy is not only supported by the MAJORITY of published laboratory studies (animal and test tube), but all of the best populations studies in the world. In other words, the countries with the healthiest lifestyle changes and diets consistently have some of the lowest risks of death from cancer and heart disease and this is really the take home message of the best selling book the China Study [9]. In other words, the healthiest foods and lifestyle changes improve life expectancy in many countries because they do not just reduce the risk of dying from 1 disease but many common diseases. Otherwise, life expectancy in these countries would be stagnant or even reduced if this was not the case.

Yet, along comes a study once in a while that receives a lot of MEDIA attention that suggests something that is heart healthy is bad for the prostate [1]! A recent study suggests that high intakes of fish or fish oil might increase the risk of aggressive prostate cancer?! What are you suppose to do right now? Please choose only one answer.

- A. Stop eating fish
- B. Stop using fish oil supplements
- C. Stop eating fish and using fish oil supplements
- D. Stop letting a single study that received a lot of media attention decide the fate of the prostate cancer world, and do not worry at all about the findings of this one study that really was NOT designed to answer this question on fish and fish oil, and in fact was not reported accurately in the media.

I choose answer “D” and I will tell you why for 3 brief reasons, and I will discuss more of this at the PCRI conference (what a teaser!).

1. Media sources reported the study and results incorrectly & the study was not originally or primarily designed to answer this question about fish oil.

If you read most of the press releases from this study it simply reports that a study of more than 3400 men found those with the highest blood percentages of omega-3 fatty acid DHA were 2.5 times more likely to develop aggressive prostate cancer compared to those with the lowest blood levels of DHA [10]. This is really inaccurate incomplete reporting of the study! This study was originally and primarily designed to test the impact of finasteride (a prescription medication) compared to placebo to determine if it can reduce the risk of prostate cancer in healthy men. The original study found that this drug can reduce the risk of non-aggressive prostate cancer but slightly INCREASES the risk of aggressive prostate cancer [11], and the FDA now agrees



that this is what the drug probably does so it has not allowed finasteride to claim that it prevent prostate cancer because the harm may outweigh the benefit in men that are healthy [12]. This is critical to understanding what is going on here. The original study was designed to test a drug that was ultimately found to increase the chances that a person would be diagnosed with aggressive prostate cancer.

Next, the researchers took all the prostate cancer cases from this study that had blood (serum) samples for omega-3 and compared them to individuals without cancer (controls) [1]. In other words, the overwhelming impact of the drug in this study, in my opinion, absolutely trumps or negates the ability to draw any definitive conclusions about whether or not certain omega-3 products increase the risk of aggressive prostate cancer. Even the authors state in the results

of their paper that the "...high-grade cases were significantly older and were more likely to have been randomized to the finasteride treatment arm." IN FACT, ABOUT TWO-THIRDS OF THE AGGRESSIVE PROSTATE CANCER CASES USED IN THE FISH OIL STUDY ALSO RECEIVED FINASTERIDE! This would completely question the findings of this study. The majority of the aggressive prostate cancer cases tied to fish oil were known to already be on a drug that significantly increases the risk of being diagnosed with aggressive prostate cancer! This same study (different publication), also reported that men in the placebo group with low cholesterol levels also had a lower risk of being diagnosed with aggressive prostate cancer, but men in the finasteride group did not [13]. In other words, one cannot ignore the power of a powerful drug to overwhelm any other results in a clinical trial. The researchers believe that this one omega-3 fatty acid was also associated with aggressive prostate cancer in the non-drug group, but in reality the number of cases were far too small to arrive at this definitive conclusion.

The next problem with the media reports might stun you, and that is the fact that it was a study that describes that over 3400 men were included but most media outlets failed to look at the paper and realize that ONLY 125 MEN WITH AGGRESSIVE PROSTATE CANCER WERE REALLY USED FOR THE PRIMARY FINDING OF THE STUDY! Let me repeat this...125 men was the total number of men diagnosed with high-grade prostate cancer, so the study results were not really about 3400 men but 125 men, and almost two-thirds of them took a drug that can increase the risk of high-grade cancer. And, how many men with high-grade cancer did not use the drug and were used in the analysis of this study? The answer is "45"! Now, you can see what small numbers were really used to arrive at the conclusions of this study and how it is easy to see that the results could be diluted or impacted by the drug or some other unknown factor making it a tough conclusion to believe.

Next, many media outlets also reported that when comparing the highest omega-3 DHA level to the lowest level groups there was a 2.5 times increase risk of aggressive prostate cancer [10], but what does this now really mean? It means that 38 high-grade cases were really compared to 15 high-grade cases to really get this result, and this is why the finding barely reached statistical significance, because the numbers

of cases in these groups are so low [1]. When you look at the 95% confidence intervals, or the statistical confidence in these findings they are all over the place or do not show confidence in the specific accuracy of this one result.

History is an important teacher here folks. Selenium supplements were originally thought to reduce the risk of skin cancer, and then it was tested in a large randomized trial and it was found that it did NOT reduce the risk of skin cancer and may have actually increased the risk of some types of skin cancer from this same trial [14,15]. However, researchers micro-analyzed the same data from this negative study and found large reductions in other cancers, such as prostate cancer based on small numbers of cases from this trial, and then they sliced and diced the blood levels to convince themselves that selenium may indeed reduce the risk of prostate cancer [14,16]. However, this was never the intention of the negative study and some 15 years later and at the cost of over 100 million dollars of tax payer money, a definitive study found that selenium did not reduce the risk of prostate cancer and may increase the risk of type 2 diabetes [8]. Vitamin E supplements followed a similar story my friends (slice and diced data and ultimately nothing). So this is similar in my opinion because the finasteride study was important, but it was a negative finding in that the risk of taking the drug for prevention only outweighs the benefit, but they slice and dice the data to draw some definitive conclusions about omega-3 fatty acids based on a small number of men! And, if this study would have shown a benefit with omega-3 in terms of lower the risk of aggressive disease I would also not be any more excited about taking fish oil or eating fish than I already am at this point in my life.

In other words, it was not study that should cause someone to change their behavior, especially since omega-3 fatty acids have been found to potentially reduce the risk of cardiovascular disease, which is the number 1 cause of death in men and women, and arguably the number 1 or 2 cause of death in men with prostate cancer [2-7]. The researchers of this study also came to the same appropriate conclusion [1]. Also, what about all those men in this study with low-grade prostate cancer? There were 1553 cases of low-grade prostate cancer, and there was NO RELATION BETWEEN OMEGA-3 BLOOD LEVELS AND CANCER RISK IN THESE MEN. I feel slightly more confident in these numbers or findings and so do the statistics. *(Continued on page 6)*

2. A quick review of omega-3 fatty acids should also make you feel better

Remember that there are 3 omega-3 fatty acids that have been shown to improve heart health and overall health [17,18]. The primary omega-3 from plants is known as ALA. The other 2 usually (not always) come from fish and fish oil supplements and are known as EPA and DHA (there are now algae based DHA supplements). However, ALA can be converted into the body into EPA and some EPA can be converted to DHA. Basically, these 3 omega-3 fatty acids are not mutually exclusive. For example, in a famous prostate cancer randomized surgery study, men that consumed foods high in ALA had significant increases in their blood EPA levels [19]! So, some plant omega-3 can be converted into fish oil omega-3 in the body. So, wouldn't a more accurate measurement of omega-3 from food and supplements come from testing the concentration of EPA + DHA (Or all 3 omega-3's) and/or looking at the intake from a food questionnaire?

When the researchers of this latest study combined the blood results of EPA and DHA in the high-grade cases they also found NO association between these 2 omega-3's and aggressive disease [1]. This again, would question the findings of DHA alone increasing aggressive disease since most healthy foods with DHA also have a good quantity of EPA, including most fish oil supplements that have more EPA actually compared to DHA. Also, researchers looked at ALA and found a non-significant lower risk of aggressive prostate cancer at the higher compared to lower blood levels! IN OTHER WORDS, WHEN YOU LOOK AT ALL OF THE 3 MOST COMMON HEALTHY OMEGA-3 COMPOUNDS IN COMBINATION, THERE WAS NO INCREASE RISK OF AGGRESSIVE PROSTATE CANCER. So, again this is data that was sliced and diced but when you look at increasing your intake of the 3 heart healthiest omega-3 fatty acids (ALA, EPA, DHA), this study does not show an increase risk of aggressive prostate cancer but perhaps a decreased risk with getting more plant omega-3 products. In fact, what the media did not know was that over the last few years researchers from this exact same study looked at combined omega-3 fatty acids from diet and supplements and found NO INCREASE RISK OF PROSTATE ENLARGEMENT OR AGGRESSIVE DISEASE [20,21]! In other words, no increased risk was found in the same study when looking at intake of omega-3

as a whole but somehow in a blood study DHA by itself is a problem? The problem here again is that most healthy foods that contain DHA also have as much or more EPA. Could there be a problem with this blood test (more on this later)?

So, be careful when you slice and dice a food product to determine if it is good or bad because it distorts the view of the forest because you are focusing on the tree. For example, for over a decade soy protein has been found to be heart healthy, but many researchers claimed that since it had plant estrogen like compounds that it was bad for breast cancer? Now, keep in mind that breast health is identical to prostate health in that almost everything heart healthy is breast healthy or may prevent breast cancer. However, soy has good protein, omega-3, nutrients, low calories, low saturated fat, fiber...it is so much more than 1 compound that may look like estrogen. Anyhow, recently the largest study of patients being treated for breast cancer found a consistent finding that soy could reduce the risk of dying from breast cancer and other disease when used with conventional breast cancer treatment [22]! And, for decades there were so many "experts" telling breast cancer patients or those worried about breast cancer to stay away from soy? Again, when looking at a problem in a vacuum it can distract you from the big picture and this is exactly what happened in this recent prostate study [1]. Fish is a wonderful lean source of protein, one of the highest natural sources of vitamin D, and one of the highest natural sources of omega-3 fatty acids (EPA and DHA), which is why the American Heart Association (AHA) recommends 2 servings of oily and fatty EPA and DHA rich fish (salmon, anchovies, mackerel, sardines, trout, herring...) and plant sources of omega-3 (this fact often gets missed) [23]. AHA also recommends 1000 mg of fish oil for those with heart disease. These are good recommendations that have and will stand the test of time.

3. While this fish story was getting attention, omega-3 and fish oils was receiving incredibly positive data throughout medicine that was completely missed!

You need to remember that medicine is like a courtroom where the majority of the evidence usually points to the right answer. It will never be unusual for a few studies to contradict findings that have been enormously and consistently positive. This is because there are 1000 of studies and probably 1000



of determinants of risk of disease and we should expect some study because of how it was designed or the population that was studied to show a different outcome. If 100 studies demonstrate that wearing a seat belt can save your life and 1 or 2 studies show that they do not, then I am not about to stop wearing a seatbelt! Perhaps those 1 or 2 studies only focused on folks going 100 miles per hour into a wall, which means that there was no way the seat belt would helped them anyway, but regardless of the reason it is the majority of the evidence that identifies the right behavior. And, again the majority of the studies on fish oil suggest that eating fish and potentially taking fish oil is not only heart healthy, but is FDA approved to reduce triglycerides (part of the cholesterol test). And, in the past few months and years have studies to suggest that omega-3 fatty acids from plants, fish, or supplements could:

- Improves most aspects of heart health [24]
- Improve vision [25]
- Improve dry eye syndrome [26]
- Improve hearing [27]
- Improves skin tone [28]

- Maintain muscle mass [29]
- Reduce kidney stone risk [30]
- Improve results when combined with a cholesterol-lowering drug [31]
- May improve pregnancy outcomes for mom and baby [32]
- May reduce hot flashes [33]
- May improve mental health [34]
- May reduce the risk of Alzheimer’s disease [35]
- May reduce the risk of diabetes [36]
- May improve erectile function [37]
- May improve fertility [38]
- May reduce risk and improve survival in prostate and other cancers [39-42]
- May improve chemotherapy results against some cancers, for example, paclitaxel-DHA (yes, the same fish oil compound in question is being attached to chemo compounds by drug companies) is a drug being tested now against multiple cancers [43]

Even when Dr. Dean Ornish showed that men on a plant based diet might reduce the risk of prostate cancer progression when on active surveillance, there were few folks that realize that men in his published study were also taking multiple supplements including high-dose fish oil as part of the protocol [44].

Yet, all you heard or read in the paper was a single study that suggested a potential negative result [1]. You have to keep in mind that most major medical centers, medical meetings, and medical journals have a public relations (PR) group that tries to constantly attract media to their group, medical center, or even discipline (medicine is a very competitive business). So, what ends up happening is that 100s of meetings, journals, and individuals in the medical field are trying to get the attention of the media and who knows what will or will not make page 1 or 6 in the local or national newspaper. What should make the paper is either a gold standard large definitive study that will change the way medicine is practiced or a good overall summary of the research on the subject. In the case of fish oil, who knew that there were so many positive studies out there throughout medicine? That is no longer an exciting story that grabs attention. Unfortunately or fortunately, the only ones that are going (Continued on page 8)

realize the objective truth about omega-3 fatty acids is you for reading this newsletter and not the 99% of the other folks that are freaking out right now because their local news source INACCURATELY reported on a single study that suggested that fish oil is unhealthy.

Finally, what about simply questioning this blood test? Why do we believe that this blood test they used in the prostate study is even an accurate predictor of healthy behavior or clinical events? There are tissue omega tests, and a red blood cell omega measurement tests, and they used a serum test (without blood cell omega concentrations) [1], but know one has tied this particular blood test used in the most recent study into concrete clinical outcomes in clinical trials. In other words, just because these individuals get a yearly or even regular blood test does not necessarily imply that it is an accurate tool to determine diet or supplement uptake or accuracy of linking these things to clinical data. There is a blood test that has been used in many studies called the “Omega-3 index” and although it is far from perfect it uses the combination of EPA + DHA in red blood cells to try and accurately predict cardiovascular risk [45]. Remember the study in question today did not find an increased risk of aggressive prostate cancer when using EPA + DHA, so had this been done there probably would have been no media story at all.

Can we learn anything from this new study?

Absolutely! I do not want to imply that it was a worthless study, but just that it should not change your healthy behaviors and the RESEARCHERS OF THIS STUDY WERE QUOTED AS SAYING THIS OVER AND OVER. In other words, it seemed the researchers probably got caught off guard with all the media attention because in their interviews they constantly reiterated that the benefits of omega-3 outweigh the negatives so keep consuming them!

I know some of the researchers from this study and they are fabulous at what they do-some of the best in the world. Perhaps we will use this study to give us more information on something that was never thought of that may become fact one day when we do get more information. For example, it is one thing to have blood levels of omega-3, but it would have been nice to also quantify prostate tissue levels of omega-3. It would have also been nice to know where these men were primarily getting their omega-3 fatty acids? Diet? Supplements?

For example, it is not unusual for some men and women to take large numbers of supplements and not rely on other healthy changes. It is also not unusual for some men and women to rely heavily on fish that are not as heart healthy such as tilapia (popular, but low in omega-3) and not follow other heart healthy behaviors in my opinion. Also, it is possible that something else or some other non-healthy behavior is increasing DHA levels alone, or there are other sources of DHA omega-3 that have not been fully researched. And, do not forget that it is also possible that the wrong blood test was used or that there is no relationship at all with this study and what increases the risk of aggressive prostate cancer. Anyhow, I think I have made my point.

Now, I have to run and go eat lunch and I am going to have a big salad with extra anchovies (I am not kidding here)! Oh, and for dinner tonight I am having salmon and some pasta with enteric-coated fish oil pills on top (okay, slight embellishment)! Heart Healthy=Prostate Healthy folks! Oh, and buckle up because I am sure that is going to be a new study soon that shows that jogging can increase your risk of getting hit by a car, playing tennis can increase your risk of getting a hand infection from a dirty racquet handle, yoga can increase your risk of a painful leg cramp, swimming can increase your risk of getting an ear infection, canoeing can increase your risk of getting a hand splinter, basketball can increase your risk of a twisted ankle, biking and horseback riding can increase your risk of erectile dysfunction, dancing can increase your risk of knee pain, and playing bingo in the winter can increase your risk of cold and flu especially if the bingo room is really crowded that day.

Dr. Moyad's Bottom Line:

Follow the American Heart Association's recommendation on eating fish. Eat fish, especially fatty fish with little to no mercury at least 2 times a week. Fish high in omega-3 and low in mercury include: Anchovies, Herring, Mackerel, Salmon, Sardines, Trout, Whitefish and I am still a fan of tuna and sushi regardless of some of the bad press that they get because the benefit exceeds the risk and I personally do not believe that I will personally get pregnant soon. When it comes to fish oil supplements, the quality control of most products is excellent because fish oil supplements are mostly derived from tiny fish. Take a fish oil supplement for a medical reason and not just because you hear that it is good for you. For example, I take 1 pill several days

a week for a little knee pain after running instead of traditional pain killers, and we recommend 1-2 fish oil pills for those on androgen deprivation treatment because of numerous benefits in reducing side effects. Do not take fish oil pills without discussing the reason you need it with the doctor you trust most. If you want an omega-3 blood test, ask for an “omega-3 index test” that combines several omega-3 fatty acids to give you a result. However, I have never really recommended such a test or had one myself (if that helps your decision making). Still, this test is getting interesting and I am keeping my eye on it.

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