

Flawed Study Seeks To Discredit Value Of Vitamin D In Preventing Prostate Cancer

On May 27, 2008, the *Journal of the National Cancer Institute* published a population-based analysis of the relationship between prostate cancer risk and serum 25-hydroxy vitamin D level in aging men.¹

The results of this population-based study prompted the study authors to conclude that vitamin D does not reduce the risk of prostate cancer, and furthermore that higher circulating levels of 25-hydroxy vitamin D may be associated with an increased risk of more aggressive forms of prostate cancer.

Given the study's surprising results, and the fact that other studies show that high levels of the active form of vitamin D have strong anti-cancer effects as well as inhibit the growth and invasion of prostate cancer cells,^{2,3,4} Life Extension's scientific team conducted a detailed review of the study.

In this rebuttal, **Life Extension** meticulously dissects the various flaws in this government-funded study. For those who don't want to read these technical details, the following is all vitamin D supplement users need to know:

Only 6.3% of the men diagnosed with prostate cancer in the study were ingesting at least 1,000 IU of dietary vitamin D daily (only 49 men out of the total of 781 men diagnosed with prostate cancer in the trial were ingesting at least 1,000 IU of vitamin D in the diet every day). Furthermore, the vitamin D **blood levels** of the study subjects were so **low** over-all that it is likely most of these study subjects took **no** supplemental vitamin D whatsoever.

Therefore, the results of this study have **no** relevance to men who are taking the recommended amounts of **vitamin D** to achieve optimal blood ranges.

The headline hungry media reported on this study as if it showed there to be no value in taking **vitamin D supplements**, when in fact it appears that the study subjects were **not** optimizing vitamin D supplementation.

As you will read, there are numerous other flaws that rendered the findings from this study utterly meaningless. Due to its publication in a government-funded journal, this study will dissuade many aging American men from taking vitamin D, which is great news for pharmaceutical companies who sell drugs to treat the multiple degenerative diseases caused by a vitamin D deficiency.

LIMITATIONS IN STUDY DESIGN – MULTIPLE SOURCES OF ERROR

When scientists interpret scientific studies, bias is an important, often overlooked source of error. In this context, bias refers to any factor in the study that may create the potential for error.

1) Of the men diagnosed with prostate cancer, a highly statistically significant ($p=0.001$) number of men had elevated PSA levels at baseline compared to the control group (mean PSA, 4.0 vs. 1.7, respectively).

Because an elevated PSA level signals the need for further work-up and evaluation, men diagnosed with prostate cancer in the study were far more likely to have a prostate biopsy than men with lower PSA levels. Therefore, the study was biased towards detection of prostate cancer in the group with higher PSA levels.

2) Of the men diagnosed with prostate cancer, a highly statistically significant ($p=0.001$) number of men had a family history of prostate cancer compared to the control group – in fact, the men diagnosed with prostate cancer in the study had a 138% greater risk of having a family history of prostate cancer.

Because family history predisposes to prostate cancer, the study was biased towards greater baseline risk of prostate cancer due to family history (genetics).

3) The time of year of blood sample collection for 25-hydroxy vitamin D was found to have a highly statistically significant effect ($p=0.001$). Levels of serum 25-hydroxy vitamin D were approximately 20% greater when collected in the summer or fall compared with the winter.

This means that there was a significant degree of variation for baseline vitamin D measurement depending upon the time of year.

4) Of the 749 men diagnosed with prostate cancer in the study, 434 were diagnosed in the second year of follow-up - fully 58% of the diagnosed prostate cancers occurred during the second year of the trial.

To place this into perspective, in order for a cancer to form a mass that is one centimeter (3/8") in diameter it must contain about 100 billion cells. A range for cancer cell doubling time is 23 to 209 days.

Assuming an average doubling time of about 3 months, this means that from the single cell stage to a one centimeter mass stage takes about 8 to 10 years. In prostate cancer, even a one millimeter-sized mass is not detectable by digital rectal exam – for prostate cancer to grow from a single cell to a one millimeter-sized mass will take about 6 years assuming a doubling time of about 100 days.

This means that a vast majority of the men diagnosed with prostate cancer in the trial already had prostate cancer when the study started.

5) The over-all median serum 25-hydroxy vitamin D level in the study was 22.4 ng/ml.

Life Extension recommends an optimal vitamin D range of at least 30 ng/ml, with the optimal level likely between 50-60 ng/ml.

Our recommendation is consistent with the current science and thought leaders in the field. For example, vitamin D authority Dr. Reinhold Vieth of the University of Toronto has argued that a blood level of at least 40 ng/mL should be achieved for optimal health.⁵ Dr. Michael Holick of Boston University has proposed that serum level of 25-hydroxyvitamin D in the range of 30-50 ng/mL is optimal for bone health and fracture prevention.⁶

So, the median 25-hydroxy vitamin D level achieved in this study (22.4 ng/ml) is far less than the recommended, optimal range 50-60 ng/ml.

6) Measurement of 25-hydroxy vitamin D was performed only once during the course of the study (baseline). However, men were diagnosed with prostate cancer up to 8 years after the start of the study. In addition, the acknowledged variability in seasonal measurement of 25-hydroxy vitamin D levels in serum was 20% in this trial.

This means that there is a high level of uncertainty with any attempt to associate a single, isolated serum 25-hydroxy vitamin D level that varies by at least 20% by time of year with prostate cancer risk over time.

Other prospective clinical studies show benefit

Three other prospective clinical studies have shown benefit with higher levels of circulating serum 25-hydroxy vitamin D and prostate cancer risk:

1) A US-based study published in 2004 showed that men in the lowest tertile (third) of plasma 25-hydroxy vitamin D level (<16 ng/ml) had a 71% greater risk of prostate cancer;⁷

2) A study published in 2000 out of Finland showed that men with 25-hydroxy vitamin D concentration below the median level of about 20 ng/ml had a 70% increased risk of prostate cancer compared to men with 25-hydroxy vitamin D levels above this level, and furthermore, that among younger men (<52 years of age), low 25-hydroxy vitamin D increased the risk of metastatic cancer by a whopping 530%;⁸

3) A 1998 US-based study showed a 20% reduced risk of prostate cancer with the highest levels (> 40 ng/ml) of serum 25-hydroxy vitamin D compared with lower levels (about 28 ng/ml).⁹

CONCLUSIONS

The current study suggesting an increase in prostate cancer risk with serum 25-hydroxy vitamin D is flawed.

From seasonal variability in vitamin D levels to detection bias associated with higher PSA levels, the study design is plagued with bias.

In addition, the inadequate over-all serum 25-hydroxy vitamin D levels achieved in the trial (approximately 22.4 ng/ml) are far below optimal levels of around 50-60 ng/mL and renders any meaningful interpretation of the trial results impossible.

- 1.Ahn J, Peters U, Albanes D, Purdue MP, Abnet CC, Chatterjee N, Horst RL, Hollis BW, Huang WY, Shikany JM, Hayes RB; For the Prostate, Lung, Colorectal, and Ovarian Cancer Screening Trial Project Team. Serum Vitamin D Concentration and Prostate Cancer Risk: A Nested Case-Control Study. *J Natl Cancer Inst.* 2008 May 27.
- 2.Skowronski RJ , Peehl DM , Feldman D . Vitamin D and prostate cancer: 1,25 dihydroxyvitamin D3 receptors and actions in human prostate cancer cell lines . *Endocrinology* . 1993 ; 132 (5): 1952 – 1960.
- 3.Peehl DM , Skowronski RJ , Leung GK , Wong ST , Stamey TA , Feldman D . Antiproliferative effects of 1,25-dihydroxyvitamin D3 on primary cultures of human prostatic cells . *Cancer Res.* 1994 ; 54 (3): 805 – 810.
- 4.Oades GM , Dredge K , Kirby RS , Colston KW . Vitamin D receptor dependent antitumour effects of 1,25-dihydroxyvitamin D3 and two synthetic analogues in three in vivo models of prostate cancer . *BJU Int* .2002 ; 90 (6): 607 – 616 .
- 5.Vieth R. Vitamin D supplementation, 25-hydroxyvitamin D concentrations, and safety. *Am.J Clin Nutr.* 1999 May;69(5):842-56.
- 6.Holick MF. The role of vitamin D for bone health and fracture prevention. *Curr Osteoporos Rep.* 2006 Sep;4(3):96-102.
- 7.Jacobs ET , Giuliano AR , Martinez ME , Hollis BW , Reid ME , Marshall JR . Plasma levels of 25-hydroxyvitamin D, 1,25-dihydroxyvitamin D and the risk of prostate cancer . *J Steroid Biochem Mol Biol.* 2004 ; 89 – 90 (1 – 5): 533 – 537.
- 8.Ahonen MH , Tenkanen L , Teppo L , Hakama M , Tuohimaa P . Prostate cancer risk and prediagnostic serum 25-hydroxyvitamin D levels (Finland) . *Cancer Causes Control* . 2000 ; 11 (9): 847 – 852 .
- 9.Nomura AM , Stemmermann GN , Lee J , et al . Serum vitamin D metabolite levels and the subsequent development of prostate cancer (Hawaii, United States) . *Cancer Causes Control* . 1998 ; 9 (4): 425 – 432 .

All Contents Copyright © 1995-2009 Life Extension Foundation All rights reserved.

LifeExtension®

These statements have not been evaluated by the FDA. These products are not intended to diagnose, treat, cure or prevent any disease. The information provided on this site is for informational purposes only and is not intended as a substitute for advice from your physician or other health care professional or any information contained on or in any product label or packaging. You should not use the information on this site for diagnosis or treatment of any health problem or for prescription of any medication or other treatment. You should consult with a healthcare professional before starting any diet, exercise or supplementation program, before taking any medication, or if you have or suspect you might have a health problem. You should not stop taking any medication without first consulting your physician.