

## Is There a Conspiracy to Destroy Vitamin Supplements?

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For the past three decades, the Life Extension Foundation has warned about an insidious relationship that exists between the federal government and pharmaceutical industry. Our position has been that this alliance represents a *conspiracy* that is largely responsible for the many problems faced by our health care system today.

On May 16, 2007, an agency of the federal government published a report that linked the use of multivitamin supplements with an increased risk of aggressive prostate cancer. The media made headline news stories out of this government-funded report, which has the unfortunate consequence of dissuading uninformed Americans from taking their vitamins. This benefits the pharmaceutical industry as vitamin deficiencies make aging humans more vulnerable to diseases that require lots of expensive prescription drugs to treat.

Even a cursory analysis of this government study reveals flaws so egregious that the findings have no meaning whatsoever. This article provides a meticulous rebuttal to this defective study. I want to point out in this introduction, however, some obvious flaws that would indicate that this study may have been deliberately designed in a way to cast a negative light on multivitamin supplements.

Just imagine if a study were conducted where ordinary people were asked to remember how much vitamin E they took each day for the past ten years. While Life Extension members might be able to recall this, the typical person randomly taking vitamin pills is unlikely to accurately recall their vitamin E dose.

In this government-funded study bashing multivitamins, the researchers had the audacity to place each subject who stated they did not know how much vitamin E they took into the 400 IU a day category. This means when the results were tabulated to see if multivitamin use was associated with prostate cancer risk, men who may or may not have taken any vitamin E were deemed to have taken 400 IU a day.

Men who reported taking even one multivitamin supplement a month were recorded as taking a multivitamin every single day. This meant that when the data was tabulated, those who may have taken as few as twelve multivitamin supplements a year were considered to have taken a multivitamin each day.

Based on the absurd design parameters established, one can clearly see that this multi-million dollar government study was designed in a way to make it *impossible* to glean any meaningful data whatsoever about the effects of multivitamins on prostate cancer risk. As you will learn in this article, there were so many flaws in this study that it should have been rejected for publication in any peer-reviewed scientific journal. Since it was published in a journal controlled by the federal government, however, it made it into the scientific arena and as a result into the mainstream media.

Life Extension has identified defects in previous studies that seek to discredit the value of dietary supplements. As you will read, this particular government-funded study may perhaps be the most error-ridden report on dietary supplements ever published.

An epidemiology study published in the *Journal of the National Cancer Institute (JNCI)* on May 16, 2007, has been heralded by many in the mainstream media as proof that multivitamin use is linked with certain aspects of prostate cancer and that specific nutritional supplements are associated with an increased risk of advanced prostate cancer.<sup>1</sup>

Although this study was observational in nature, that did not stop the headline-hungry mainstream media from misrepresenting the results and conclusions of this study. As lead study author Michael F. Leitzmann, MD, from the National Cancer Institute was quoted as saying:

*"This was an observational study, and so no conclusions can be drawn about cause and effect. For this reason, we must be cautious in giving any firm advice based on the results of this study."*<sup>2</sup>

## **A QUESTIONNAIRE-BASED OBSERVATIONAL STUDY THAT DID NOT TEST FOR CAUSALITY**

This recent population-based analysis used questionnaires and prostate cancer patient recall/memory as a basis of data collection. Questionnaire-based information collection is limited in accuracy to the memory recall of the study subjects. The majority of people cannot recall what they ate for breakfast one week ago, or which shirt they wore to work two weeks ago, or how many gallons of gas they purchased during their last trip to the gas station, never mind specific doses and frequency of use of a myriad of dietary supplements months or years ago.

*Data dredging*, also known as *data mining*, involves using mathematical techniques to sift through large amounts of historical information to try and patch together associations between bits and pieces of data. These types of techniques look for associations, not causal relationships. Contrast this emphasis on testing for associations versus the use of direct-intervention studies. Direct-intervention studies evaluate the direct effect of an intervention in a population over time thus, direct-intervention studies assess for cause and effect relationships.

An example of data dredging/data mining would be to look at different groups of patient characteristics (for example, patients who recall consuming five alcoholic drinks per week, patients who remember eating more than 10 servings of vegetables a week, patients who attend religious services at least 25 times per year, etc.) in an insurance company's HMO database to see which set of characteristics was more associated with the development of lung cancer. On the other hand, an example of a direct-intervention study would be to give a group of patients a particular drug, and then study how many lung cancers were prevented by this drug over time.

The recent questionnaire-based observational study employed the use of data dredging/data-mining techniques, and did not study the direct intervention of supplements on prostate cancer risk.

## **BETTER-QUALITY HUMAN CLINICAL STUDIES SHOW A PROTECTIVE EFFECT**

Fortunately, there are a wealth of other prostate cancer prevention studies that use rigorous and well-defined design criteria. The following studies suggest significant benefits from selenium and other antioxidant supplements, such as beta-carotene and the gamma-tocopherol fraction of vitamin E:

- A 1996 study from the Nutritional Prevention of Cancer Study Group showed that patients treated with 200 mcg of selenium had a significant 50% reduction in total cancer mortality, a 37% reduction in total cancer incidence, and a reduction in the risk of lung, colorectal, and prostate cancers.<sup>3</sup>
- A 1998 double-blind, placebo-controlled trial showed that 200 mcg of selenium significantly decreased the risk of prostate cancer by 63% over an average of 4.5 years of treatment and an average follow-up of 6.5 years. Furthermore, there were significant health benefits for total cancer mortality and the incidence of total lung and colorectal cancer.<sup>4</sup>
- The SU.VI.MAX trial was composed of 5,141 men followed over eight years, and it evaluated antioxidant vitamin and mineral supplementation and prostate cancer prevention. Among aging men with a normal PSA count, there was a marked, statistically significant 48% reduction in the rate of prostate cancer for men receiving the antioxidant supplements.<sup>5</sup>
- The Physicians' Health Study, a randomized, double-blind, placebo-controlled trial, examined dietary supplementation in the primary prevention of cancer among 22,071 US male physicians ages 40–84. Men experienced a significant 32% reduction in the risk of prostate carcinoma with 50 mg of beta-carotene supplementation.<sup>6</sup>
- The Alpha-Tocopherol, Beta-Carotene Cancer Prevention Study (ATBC) demonstrated a 32% reduction in prostate cancer risk in response to daily vitamin E supplementation. Also, participants with higher circulating concentrations of the important gamma-tocopherol form of vitamin E had lower prostate cancer risk.<sup>7</sup>

In addition, high levels of serum selenium have been associated with a 29% decreased risk of prostate cancer (comparing highest to lowest quartiles for serum selenium), and analysis of serum selenium levels indicates a reduced risk of prostate cancer with selenium levels above concentrations of 0.135 mcg/mL (median value), with additional benefit for selenium among men with low serum alpha-tocopherol concentrations.<sup>8</sup>

Moreover, a recent study also demonstrated that higher serum selenium may be associated with reduced prostate cancer risks in men who reported a high intake of vitamin E, as well as in multivitamin users.<sup>9</sup>

## **DOSE-COLLECTION TECHNIQUES RAISE ACCURACY CONCERNS**

The recent *JNCI* questionnaire-based study used arbitrary dose assignment for unknown dosing of vitamin E, as well as other low-stringency criteria for other multivitamins.

Taken verbatim from the questionnaire-based observational study:

*“Each category of (vitamin E) dose was assigned as 100, 200, 400, and 800 IU, and for those answering “unknown,” a value of 400 IU was assigned.”*

*“For those taking a multivitamin, daily dose of supplemental vitamin E was assumed to be 30 IU” and “Use of iron, zinc, selenium, and folic acid was assessed by asking participants whether or not they used each of these individual supplements more than once per month in the past 12 months (yes or no).”*

If a man used iron, selenium, or folate supplements once per month in the past 12 months, how can this be reliable for ascertaining dose or compliance? If a man could not remember a specific dose of vitamin E used, then how is any dose accuracy possible if men are arbitrarily assigned a dose of 400 IU of vitamin E?

Life Extension has long reported the importance of the gamma-tocopherol fraction of vitamin E and the suboptimal benefits of using only alpha-tocopherol supplementation, yet this questionnaire-based study made no attempt to record gamma-tocopherol dosing.

**Amazingly, despite these inherent dosing inaccuracies, the mainstream media was quite content to argue that supplements such as vitamin E and selenium are linked with advanced prostate cancer risk.**

### The overall analysis showed no evidence of a trend for increased risk of prostate cancer in any category of multivitamin frequency

The primary analysis in this questionnaire-based study did not show evidence of risk of prostate cancer (Table 2 copied directly from the study—below), yet this fact was not reported by the headline-hungry mainstream media. Rather, the media chose to emphasize convoluted subgroup analyses to sensationalize contrived statistical associations.

In none of the categories in Table 2 (below) from the study, including advanced prostate cancer, were any of the p-values (probability values) for trends across categories significant:

**Table 2.** Relative risks and 95% confidence intervals for prostate cancer according to frequency of multivitamin use in the National Institutes of Health–AARP Diet and Health Study\*

Prostate cancer	Frequency of multivitamin use, no. of times per week				P <sub>trend</sub>
	Never	1–6	7	>7	
<b>Total†</b>					
No. of cases/person-years	4931/11 895	1050/2547	3768/8952	492/1139	
Age-adjusted RR (95% CI)	1.00 (ref)	0.98 (0.92 to 1.05)	1.02 (0.97 to 1.06)	1.05 (0.96 to 1.16)	.30
Multivariable RR‡ (95% CI)	1.00 (ref)	0.97 (0.91 to 1.04)	1.02 (0.98 to 1.07)	1.06 (0.97 to 1.17)	.20
<b>Localized†</b>					
No. of cases/person-years	4231/10 357	887/2201	3240/7818	407/971	
Age-adjusted RR (95% CI)	1.00 (ref)	0.97 (0.90 to 1.05)	1.02 (0.97 to 1.06)	1.02 (0.92 to 1.13)	.49
Multivariable RR‡ (95% CI)	1.00 (ref)	0.96 (0.89 to 1.03)	1.02 (0.97 to 1.07)	1.02 (0.92 to 1.14)	.39
<b>Advanced†</b>					
No. of cases/person-years	700/1538	163/346	528/1 134	85/168	
Age-adjusted RR (95% CI)	1.00 (ref)	1.05 (0.89 to 1.25)	1.01 (0.90 to 1.13)	1.27 (1.02 to 1.59)	.30
Multivariable RR‡ (95% CI)	1.00 (ref)	1.05 (0.88 to 1.25)	1.03 (0.91 to 1.16)	1.32 (1.04 to 1.67)	.21
<b>Fatal‡</b>					
No. of deaths/person-years	90/331	20/67	55/218	14/58	
Age-adjusted RR (95% CI)	1.00 (ref)	1.07 (0.66 to 1.73)	0.80 (0.57 to 1.12)	1.65 (0.94 to 2.91)	.84
Multivariable RR‡ (95% CI)	1.00 (ref)	1.18 (0.71 to 1.94)	0.90 (0.63 to 1.29)	1.98 (1.07 to 3.66)	.65

\* RR = relative risk; CI = confidence interval; ref = referent category.

† Based on up to 5 years of follow-up time (1995–2000).

‡ Adjusted for body mass index; height; age; family history of prostate cancer; education; race; smoking status; physical activity; marital status; intakes of tomato and tomato products, fish, red meat,  $\alpha$ -linolenic acid, dietary calcium, individual calcium supplement, dietary vitamin D, dietary zinc, individual zinc supplement, dietary vitamin E, individual vitamin E supplement, and alcohol; and personal history of diabetes.

§ Based on up to 6 years of follow-up time (1995–2001).

### STUDY DESIGN BIAS AGAINST MULTI-VITAMINS

Most, if not all, epidemiological studies are subject to bias of one sort or another. It is important to assess the probable impact of bias on outcomes. There are several forms of bias in this questionnaire-based study that affected the observed associations.

In this study, a family history of prostate cancer was associated with supplement use, and prostate cancer PSA screening was most frequent among heavy users of multivitamins, consistent with other survey data showing that men who used supplements were more likely to have PSA examinations than nonusers. Therefore, there is increased prostate cancer *detection* among this subpopulation of men who are heavy supplement users and who are more likely to seek health care tests owing to a positive family history of prostate cancer. This is a form of **detection or diagnosis bias**.

As the authors accurately said (but the mainstream media did not report):

“ .it is possible that the positive association with heavy use of multivitamins along with certain supplements was spurious... and  
“ .the increased risk of localized prostate cancer among men with heavy multivitamin use and concomitant use of a selenium or folate supplement in our study may be due to similar **diagnostic bias**... ”

In fact, when excluding men diagnosed with prostate cancer within the initial two years of the study period, the relative risk of advanced prostate cancer with heavy multivitamin use no longer existed.

Men with a family history of prostate cancer are also more likely to consume dietary supplements for prostate health, further confounding the interpretation of the overall data analysis in this questionnaire-based study. Family history of prostate cancer is itself a recognized risk factor for prostate cancer development.

### LACK OF BIOLOGICAL PLAUSIBILITY

Even assuming that the results from this flawed, questionnaire-based study are accurate, there remains the question of biologic plausibility. In other words, is there a plausible mechanism that can explain why or how these study results could occur?

**Vitamin E, beta-carotene, and vitamin C are micronutrient antioxidants that protect cells from oxidative damage involved in prostate carcinogenesis. For example, in a separate trial**, supplemental vitamin E was associated with a decreased risk of prostate cancer among smokers, and supplemental beta-carotene was associated with a decreased risk of prostate cancer among men with low baseline plasma beta-carotene levels, while beta-carotene intake at a dose level of at least 2000 mcg/day was associated with a 48% decrease in prostate cancer risk in men with low (below the median of 4,129 mcg/ day) dietary beta-carotene intake.<sup>10</sup>

**Although selenium and alpha-tocopherol (the major form of vitamin E in supplements) appear to have protective effects against prostate cancer, little attention has been paid by scientific researchers to *gamma-tocopherol*.** A case in point is a study that examined the associations of alpha-tocopherol, gamma-tocopherol, and selenium with incident prostate cancer. The results showed that the risk of prostate cancer declined with *increasing* concentrations of alpha-tocopherol. For gamma-tocopherol, men in the highest fifth of the distribution had a powerful five-fold *reduction* in the risk of developing prostate cancer than men in the lowest fifth of the distribution. Statistically significant protective associations for high levels of selenium and alpha-tocopherol were observed *only* when gamma-tocopherol concentrations were high.<sup>11</sup> The men participating in the study claiming that multivitamins increased aggressive prostate cancer risk were not obtaining *any* gamma tocopherol in supplement form.

### Cancer industry profits require lots of cancer victims

The “cancer industry” is gigantic. Like any other business, profits are dependent on consistent and predictable volume. The *American Cancer Society* predicts that **1,444,920 people** will be diagnosed with cancer in the United States in year 2007.

Those involved in the “cancer industry” have a huge financial stake in **1,444,920 Americans** contracting cancer this year. A substantial body of research, however, indicates that these cancer rates could be sharply reduced. For example, very strong evidence indicates that higher-potency vitamin D supplements could cut the rate in which people contract cancer by **50%** or more. Yet the federal government makes it *illegal* for those who sell vitamin D supplements to make a cancer claim on the label of their product, thereby denying this knowledge to the majority of Americans.

If cancer incidences did decline by 50%, an enormous economic upheaval would occur throughout the “cancer industry”. There is thus a huge economic bias in keeping Americans in the dark about what they can do to reduce their risk of contracting cancer.

The amount of vitamin D contained in the multivitamin supplements taken by participants in the study that claimed an increased risk of aggressive prostate cancer was small, as were the potencies of selenium, vitamin E and other nutrients. In response to the many favorable reports about vitamin D, we expect the makers of multivitamins to add more vitamin D to their formulas, as it takes up virtually no space and costs very little.

The problem is that fewer Americans are likely to take these multivitamin supplements based on the wildly distorted stories disseminated by the media (based on this horribly flawed government-published study). The cancer industry’s public relations

machine thus ensures a continuous flow of new patients who will require surgery, radiation, chemotherapy, and a host of other super-expensive drugs. Good financial news for the cancer industry, but disastrous for the 1.4 million individuals who face the nightmare of mutilating and toxic treatments that too often fail to cure the disease.

**As educated health consumers, Life Extension members learn the hard facts as to what may or may not prevent cancer. Our fear is that the effect of this recent questionnaire-based observational study will both deter men from aggressive prostate health and cancer prevention strategies, and quell future research on dietary supplementation and prostate cancer risk.**

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