

## Response to SELECT Study Published December 9, 2008 in JAMA

The Selenium and Vitamin E Cancer Prevention Trial (SELECT) examined the effects of L-selenomethionine and all-racemic alpha-tocopherol acetate, alone or in combination, on the risk of prostate cancer and other health outcomes in relatively healthy men. The trial included 35,533 men (age 50 years or older for African-American men and age 55 years or older for other men at the start of the study), from the U.S. and Canada, and Puerto Rico. The participants were randomly assigned to receive one of four interventions between August 2001 and June 2004 for a planned minimum follow-up of 7 years: L-selenomethionine (200 micrograms per day) and a vitamin E placebo; all-racemic alpha-tocopheryl acetate (400 IU/day) and a selenium placebo; L-selenomethionine plus all-racemic alpha-tocopheryl acetate; or a placebo.

The researchers reported that there were no statistically significant differences in the absolute number (or 5-year incidence rate) of prostate cancer diagnosis between the four groups.

**In January, 2008, as part of the article “Merv Griffin’s Tragic Death From Prostate Cancer,” Life Extension predicted that SELECT would fail, and furthermore, that this flawed trial would be misused by the pharmaceutical monopoly and the mainstream medical establishment to “prove” to the lay public that low-cost, efficacious nutrients like vitamin E and selenium do not reduce prostate cancer risk,<sup>1</sup> and by extrapolation, to impugn other low-cost, efficacious nutrients like vitamin D, selenium, fish oil, and soy as having no benefit.**

For example, other clinical studies with selenium supplements show strong benefit in prostate cancer as well as a variety of other deadly cancers:

- A study of 1,312 individuals who received 200 mcg of selenium daily or a placebo showed almost 50% lower risk of prostate cancer in the supplemented group than in the control group in men who had relatively low prostate-specific antigen (PSA) levels and low initial selenium levels.<sup>2</sup>
- A study of 5,141 men taking a selenium-containing supplement or a placebo for eight years, with biochemical markers of prostate disease measured at the beginning and end of the study, showed that among men who had normal PSA levels at the study’s outset, a significant risk reduction of nearly 50% was recorded.<sup>3</sup>
- A 2005 study focusing on selenium’s effects in preventing prostate cancer in patients with early prostate cancer took selenium, vitamin E, both L-selenomethionine and vitamin E, or a placebo for three to six weeks before undergoing prostatectomy (removal of the prostate). Levels of cancer markers were measured and compared with healthy control subjects. The result was a change in classification from cancerous to healthy in the serum markers of disease in the men who took supplements compared to those who did not.<sup>4</sup>
- A study in men at high risk of lung cancer with low dietary selenium intake were randomly assigned to receive either 300 mcg of selenium or a placebo daily for one year. As expected, selenium blood levels rose dramatically in the supplemented group, while serum levels of the antioxidant enzyme glutathione peroxidase increased by 156%. At the same time, levels of lipid peroxide (a measure of cell membrane damage that leads to cancer) were reduced by 75% in the supplemented group, and there was laboratory evidence of protection from DNA damage, another prerequisite for cancer formation.<sup>5</sup>
- The US Nutritional Prevention of Cancer Trial demonstrated a statistically significant reduction in lung cancer incidence with selenium supplementation, with 200 micrograms per day cutting the incidence of cancer by nearly 50%.<sup>6</sup> A later re-analysis with additional data showed the effect to be most significant in people with low baseline selenium levels, again suggesting that supplementation is preventive when initiated early.<sup>7</sup>

**Life Extension has conducted a thorough review of this latest study used to attack dietary supplements. In fact, Life Extension’s members were made aware of a fundamental fact 8 years ago that all but guaranteed trial failure of this latest attack against dietary supplements.**

**In the current JAMA trial, men supplemented with all-racemic alpha-tocopherol experienced significant gamma-tocopherol depletion. A careful review of the actual full-text JAMA publication reveals gamma-tocopherol depletion among those men supplemented with all-racemic alpha-tocopherol. Men supplemented with all-racemic alpha-**

**tocopherol and alpha-tocopherol plus selenium experienced a 45% and 48%, respectively, depletion in gamma-tocopherol levels by 6 months that was sustained during the course of this 5-year trial.**

**As far back as March, 2001 in the article “Avoiding Prostate Cancer,”<sup>8</sup> Life Extension identified the importance of gamma-tocopherol supplementation in dramatically lowering the risk of developing prostate cancer — in fact, a study of 10,456 men showed that men who had the highest blood levels of gamma-tocopherol were five times less likely to get prostate cancer.<sup>9</sup>**

What made this study particularly significant was that it was conducted at the prestigious Johns Hopkins School of Public Health and it evaluated a large group of men over a seven-year period. In addition to the finding that higher levels of gamma-tocopherol significantly reduced prostate cancer risk, the study showed that selenium and alpha-tocopherol also reduced prostate cancer incidence, but only when gamma-tocopherol levels are high.

Gamma-tocopherol is a form of vitamin E that is lacking in almost all commercial vitamin E supplements. When high doses of alpha-tocopherol vitamin E are consumed, it displaces critically important gamma-tocopherol in the cells. While alpha-tocopherol inhibits the production of free radicals, it is the gamma-tocopherol form of vitamin E that is required to trap and neutralize free radicals. In a study published in the *Proceedings of the National Academy of Sciences*,<sup>10</sup> researchers reported that it could be dangerous to take high levels of alpha-tocopherol vitamin E without also consuming gamma-tocopherol. The reason for this is that too much alpha-tocopherol could deprive the cells of the gamma form of vitamin E that is needed to neutralize existing oxidizing agents such as the peroxynitrite radical, which can be especially damaging.

The scientists who wrote the National Academy of Sciences article suggested that alpha-tocopherol vitamin E supplements should contain at least 20% tocopherol. In response to these recommendations, Foundation members began taking one capsule a day of a supplement called Gamma E Tocopherol that provided 210 mg of gamma-tocopherol in each capsule. This same amount of gamma-tocopherol (210 mg) was later added to the Life Extension Booster formula. Foundation members obtained additional protection in the Super CoQ10 softgel caps that are fortified with a tocotrienol complex that provides the gamma-tocotrienol vitamin E fraction.

The average Life Extension member takes at least 400 IU a day of alpha-tocopherol. The 237 mg of gamma-tocopherol found in ‘Gamma E Tocopherol with Sesame Lignans’ or the 215–244.2 mg gamma-tocopherol found in our ‘Super Booster’ helps our members easily exceed the 20% gamma-tocopherol threshold. Furthermore, many of our members achieve a 1:1 ratio of alpha-gamma-tocopherol ingestion, a ratio suggested as ideal by expert research groups in vitamin E such as Bruce Ames’ laboratory at UC Berkeley.<sup>11</sup>

Other nutrients like vitamin D, along with what a man eats, have a huge impact on prostate cancer incidence. Unless these powerful confounding factors are carefully accounted for, the findings from this selenium-alpha-tocopherol study will have little value.

**The landmark article “Eating Your Way to Prostate Cancer” published February, 2007 in *Life Extension* magazine (reviewed and critiqued by Scientific Advisory Board member Stephen Strum, MD a recognized authority on prostate cancer prevention and treatment) reported the importance of controlling dietary intake of arachidonic acid and the grave consequences of failing to mitigate up-regulation of the 5-LOX enzyme by poor dietary choices.<sup>12</sup>**

This fact reveals a fundamental problem confronting all researchers who seek to “prove” whether a certain supplement prevents a disease. There are too many factors involved in the development and progression of prostate cancer including low levels of testosterone, increased levels of estrogen, co-existing diabetes or metabolic syndrome, and increased dietary saturated fats.<sup>13</sup> These confounding factors therefore make it difficult to study just one or two compounds and expect to come up with a validated finding. To make matters worse, the aging population will contract prostate cancer at epidemic levels unless aggressive changes are implemented immediately.

This is why we encourage Foundation members to consume the healthy diets and safe supplements that have been shown to sharply reduce prostate cancer incidence. There is simply not enough time left in our generation’s projected life spans to withstand scientific study design flaws, the mainstream medical establishment’s bias against supplements, and arbitrary standards set by the pharmaceutical monopoly.

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