

Selenium and vitamin E supplementation over recommended dietary intake may raise prostate cancer risk

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A multi-center study led by Fred Hutchinson Cancer Research Center has found that high-dose supplementation with both the trace element selenium and vitamin E increase the risk of high-grade prostate cancer. But importantly, this risk depends upon a man's selenium status before taking the supplements.

These findings, published in *Journal of the National Cancer Institute*, are based on data from the Selenium and Vitamin E Cancer Prevention Trial, or SELECT, a rigorously executed, randomized and placebo-controlled trial that involved more than 35,000 men. The study sought to determine whether taking high-dose vitamin E (400 IU/day) and/or selenium (200 mcg/day) supplements could protect men from prostate cancer.

The trial, which began in 2001 and was designed to last 12 years, stopped early, in 2008, because it found no protective effect from selenium and there was a suggestion that vitamin E increased risk. While use of the study supplements stopped, men were still followed and after an additional two years the men who took vitamin E had a statistically significant 17 percent increased risk of prostate cancer.

Selenium supplementation increased cancer in men with high selenium status at baseline

When the study started, there was some evidence that selenium supplementation would not benefit men who already had an adequate intake of the nutrient. For that reason, researchers measured the concentration of selenium in participants' toenails and planned to test whether selenium supplementation would benefit only the subset of men with low selenium status at baseline. Instead, they found that taking selenium supplements increased the risk of high-grade cancer by 91 percent among men with high selenium status at baseline. When selenium supplements were taken by men who had high selenium status to begin with, the levels of selenium became toxic.

Taking vitamin E increased cancer risk in men with low selenium status at baseline

The study also found that only a subgroup of men was at increased risk of prostate cancer from taking vitamin E. Among men with low selenium status at baseline, vitamin E supplementation increased their total risk of prostate cancer by 63 percent and increased the risk of high-grade cancer by 111 percent. This explained one of the original SELECT findings, which was that only men who received vitamin E plus a placebo pill, and not those who received both vitamin E and selenium, had an increased prostate cancer risk. Selenium, whether from dietary sources or supplements, protected men from the harmful effects of vitamin E.

"Many people think that dietary supplements are helpful or at the least innocuous. This is not true," said corresponding and first author Alan Kristal, Dr.P.H., a faculty member in the Public Health Sciences Division of Fred Hutch. "We know from several other studies that some high-dose dietary supplements – that is, supplements that provide far more than the daily recommended intakes of micronutrients – increase cancer risk. We knew this based on randomized, controlled, double-

blinded studies for folate and beta carotene, and now we know it for vitamin E and selenium."

The data for the current analysis compared the effect of selenium and vitamin E, taken either alone or combined, on prostate cancer risk among 1,739 men who were diagnosed with prostate cancer and, for comparison purposes, a random sample of 3,117 men without prostate cancer who were matched to the cases by race and age.

The bottom line: The study showed no benefits to any men from either selenium or vitamin E supplements, and for significant proportions of men in the study these supplements were harmful.

"These supplements are popular – especially vitamin E – although so far no large, well-designed and well-conducted study has shown any benefits for preventing major chronic disease," Kristal said.

No known benefits – only risks

"Men using these supplements should stop, period. Neither selenium nor vitamin E supplementation confers any known benefits – only risks," he continued. "While there appear to be no risks from taking a standard multivitamin, the effects of high-dose single supplements are unpredictable, complex and often harmful. Taking a broad view of the recent scientific studies there is an emerging consistency about how we think about optimal intake of micronutrients. There are optimal levels, and these are often the levels obtained from a healthful diet, but either below or above the levels there are risks."

Provided by Oxford University Press

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