

## **Selenium and Vitamin E Cancer Prevention Trial (SELECT): Questions and Answers**

### **Key Points**

- SELECT stands for the Selenium and Vitamin E Cancer Prevention Trial, a clinical trial to see if one or both of these dietary supplements prevent prostate cancer (see Question 1).
- Selenium and vitamin E are antioxidants. Earlier studies suggested that these supplements might prevent prostate cancer (see Questions 3, 4, and 5).
- In order to participate in SELECT, men had to meet certain eligibility requirements (see Questions 6, 7, and 8).
- Men who participate in this study were randomly assigned to take two capsules a day—selenium and vitamin E, selenium and a placebo, vitamin E and a placebo, or two placebos (see Question 10).
- Participants are asked to provide toenail and blood samples, respond to an annual questionnaire, and pick up capsules every 6 months (see Question 13).

### **1. What is SELECT?**

SELECT stands for the Selenium and Vitamin E Cancer Prevention Trial, a clinical trial to see if one or both of these dietary supplements prevent prostate cancer. The trial is funded by the National Cancer Institute (NCI) and is being coordinated by the Southwest Oncology Group (SWOG), an international network of research institutions that receives NCI funding. Enrollment began in 2001 and ended in 2004, 2 years ahead of the originally planned 5 years. The study will continue for 7 years after the last man enrolled, meaning that each man will participate for 7 years or more, depending on when he joined the study. More than 400 sites in the United States, Puerto Rico, and Canada are taking part in the study. Over 35,000 men are participating in SELECT.



**2. What are a man's chances of developing prostate cancer?**

Except for skin cancer, prostate cancer is the most common type of cancer in men in the United States. In 2005, there will be an estimated 232,090 new cases of prostate cancer and 30,350 deaths from this disease in the United States (1).

Approximately 1 in 6 men in the United States (or 17.8 percent) will develop prostate cancer during his lifetime (1). All men are at risk, but those at highest risk fall into one or more of the following categories: age 55 or older; black; or have a father or brother with prostate cancer.

**3. What is selenium? Why study it for prostate cancer prevention?**

Our bodies need selenium, a nonmetallic trace element that we get from food—especially plant foods like rice and wheat, seafood, meat, and Brazil nuts. Selenium is an antioxidant that might help control cell damage that can lead to cancer.

The Nutritional Prevention of Cancer Trial, published in 1996, included 1,312 men and women who had skin cancer. Men who took selenium to prevent nonmelanoma skin cancer received no benefit from selenium in preventing skin cancer. However, men who had taken selenium for 6½ years had approximately 60 percent fewer new cases of prostate cancer than men who took the placebo (2). In 2002, study data showed that men who took selenium for more than 7½ years had about 52 percent fewer new cases of prostate cancer than men who took the placebo (3). This study is one of the reasons selenium is being studied in SELECT. (See Question 11 for more information about selenium.)

**4. What is vitamin E? Why study it for prostate cancer prevention?**

We get vitamin E in a wide range of foods, especially vegetables, vegetable oils, nuts, and egg yolks. Vitamin E, like selenium, is an antioxidant, which might help control cell damage that can lead to cancer.

In a 1998 study of 29,133 male smokers in Finland, men who took vitamin E to prevent lung cancer had 32 percent fewer new cases of prostate cancer than men who took the placebo. Some men also took beta carotene, but neither substance helped prevent lung cancer (4). (See Question 12 for more information about vitamin E.)

**5. What do researchers hope to learn from SELECT?**

SELECT is the first study to look directly at the effects of selenium and vitamin E on the risk of prostate cancer. This study is designed to find out if selenium, vitamin E, or both prevent prostate cancer.

A large trial of selenium and vitamin E is needed to substantiate earlier, separate findings from studies in which prostate cancer was not the primary outcome. Although two earlier

studies suggested that these two supplements might prevent prostate cancer, this cancer was not the focus of those studies. The primary goal of SELECT is to assess the effect of these substances on the number of new cases of prostate cancer diagnosed during routine clinical practice. Other objectives are to assess the impact of selenium and vitamin E on the incidence of lung and colon cancer, as well as on survival. SELECT will study the molecular genetics of cancer risk and associations between diet and cancer. Additionally, SELECT will examine quality of life.

**6. Who was eligible to participate in SELECT? Were there restrictions on eligibility?**

Many diseases, including prostate cancer, occur more frequently in older persons. The risk of developing prostate cancer increases with age. More than 92 percent of prostate cancer cases occur in men age 55 and older.

Black men had to be age 50 or older to participate, and men of other races and ethnicities had to be 55 or older. The age for eligibility was lower for black men because, on average, they get the disease at an earlier age. In addition, black men in the United States have the highest incidence of prostate cancer in the world. Thus, the SELECT age requirement ensured that men at risk for the disease were the ones who could enroll.

Men who had taken, or were taking, vitamin E and/or selenium on their own had to stop using these supplements and any multivitamins and use only what is provided by SELECT. These supplements are provided to participants free of charge, including a multivitamin that does not contain vitamin E or selenium. Past use of these supplements did not disqualify men from joining SELECT.

Participants must have had no history of prostate cancer. Men who joined SELECT also must not have had any other cancer, except nonmelanoma skin cancer, in the last 5 years. They must have been in generally good health. Many of the 18,000 men who participated in another prevention study sponsored by NCI and run by SWOG, known as the Prostate Cancer Prevention Trial (PCPT), were eligible to participate in SELECT if they had no evidence of prostate cancer.

Some SELECT study sites are located at Veterans Administration hospitals run by the Department of Veterans Affairs. Veterans could enroll at these sites even if they did not receive their routine medical care at that hospital.

**7. Could men with benign prostatic hyperplasia (BPH) join SELECT?**

Men with BPH, an abnormal growth of benign prostate cells, could join SELECT because BPH is not a cancerous or precancerous condition. In BPH, the prostate grows larger and presses against the urethra and bladder, interfering with the normal flow of urine. More than half of the men in the United States between the ages of 60 and 70, and as many as 90 percent of men between the ages of 70 and 90, have symptoms of BPH.

BPH can be treated with four different FDA-approved drugs: finasteride (Proscar®), terazosin (Hytrin®), doxazosin (Cardura®), and tamsulosin (Flomax®). Most men taking one of these drugs were eligible to participate in SELECT.

## **8. What tests were used to determine eligibility for SELECT?**

Tests included a digital rectal examination (DRE) and a prostate-specific antigen (PSA) test. During a DRE, a doctor inserts a gloved finger into the rectum and feels the prostate gland through the rectal wall to check for bumps or abnormal areas. The PSA test measures the level of PSA (a protein produced by the cells of the prostate gland) in the blood. PSA levels can rise due to cancer or benign (not cancerous) conditions. Doctors often use the PSA test and DRE as prostate cancer screening tests in men who have no symptoms of the disease.

To be eligible for the SELECT trial, participants had to have a DRE that found no signs of prostate cancer and a total PSA level less than or equal to 4.0 ng/ml.

During the trial, DREs and PSA tests are suggested, but not required, on an annual basis throughout the course of the study.

## **9. Who pays for these tests?**

Physician, medical examination, and general clinic costs, including DREs, are charged to the participant in the same way as if he were not part of the trial. These costs may be covered by a participant's health insurance. Financial assistance may be available for some men. SELECT, however, pays for follow-up PSA tests. Men with questions about insurance coverage or reimbursement should check with their local SELECT site.

## **10. Who gets which supplement?**

Men who participate in this study take two capsules a day. Participants were randomized (assigned by chance) to receive:

- selenium and vitamin E
- selenium and a placebo
- vitamin E and a placebo
- two placebos

Two placebos are used in the trial: one looks and tastes like a selenium capsule; the other looks and tastes like a vitamin E capsule. Each placebo contains only inactive ingredients. Neither the participants nor the researchers will know who is receiving the selenium and vitamin E, or the placebos, until the end of the study.

DSM Nutritional Products, Inc. (formerly Roche Vitamins, Inc.), Parsippany, New Jersey, is donating bulk vitamin E and vitamin E placebo oils; Tishcon Corporation,

Westbury, New York, is currently encapsulating the vitamin E and vitamin E placebo; and Sabinsa Corporation, Piscataway, New Jersey, is providing selenium and selenium placebo capsules at cost.

**11. How much selenium is being used in SELECT? What risks might be involved?**

The amount of selenium (provided as l-selenomethionine) is 200 micrograms ( $\mu\text{g}$ ) daily. Although the initial results of the Nutritional Prevention of Cancer Trial showed an overall decrease in cancer incidence from selenium, a 2003 update reported 17 percent more new nonmelanoma skin cancers in the selenium group compared with the placebo group (5). It is not clear how these results would apply to men who did not already have skin cancer when they enrolled in SELECT, or to men who are not at increased risk for skin cancer.

**12. How much vitamin E is being used in SELECT? What risks might be involved?**

The amount of vitamin E (provided as dl-alpha-tocopherol acetate) is 400 milligrams (mg), which is equivalent to 400 International Units (IU) per day. This dose of vitamin E can thin the blood somewhat. Men with uncontrolled high blood pressure were not eligible to take part in SELECT because taking this much vitamin E might have increased their risk of stroke.

Vitamin E has been shown to increase the risk of some cardiovascular conditions. In a 2005 study, men and women with vascular disease or diabetes who took 400 IU of vitamin E daily for 7 years had a 13 percent increased risk of heart failure compared with participants taking a placebo (6). Heart failure is a condition in which the heart's ability to pump blood is weakened. A 2005 analysis of several studies in which people with various medical problems took vitamin E suggested a link between high doses of vitamin E (400 IU or more) and increased mortality (7).

**13. What other requirements were there for SELECT participants?**

Upon enrollment, men were asked to have toenail clippings collected to assess selenium levels in the body because selenium concentrates in fingernails and toenails. Toenails were chosen over fingernails because they take longer to grow and thus contain more history of someone's selenium intake. Blood samples were collected upon enrollment to assess levels of vitamin E.

Upon enrolling, men filled out a questionnaire on their diet and past supplement use. There is also an annual questionnaire that asks for updates of some of this information. Men do not have to change their diets during this study. Each man is offered a supply of a special daily multivitamin, manufactured by The Perrigo Company, Allegan, Michigan, that contains no selenium or vitamin E, to take if he chooses. Vitamin E, selenium, placebo capsules, and multivitamins will be provided free of charge to enrollees for the duration of the study.

Participants are asked to return to the study site every 6 months to pick up a 6-month supply of capsules.

**14. What are the benefits of participating in SELECT?**

Men involved in SELECT are partners in medical research that may decrease their chances of getting prostate cancer. Information learned from this study may also help future generations of men avoid this cancer.

**15. What happens if a participant develops prostate cancer while involved in SELECT?**

Participants diagnosed with prostate cancer during the study will be referred for treatment, will stop taking the study supplements, and will continue to be followed by the SELECT study staff, although less frequently.

Costs for diagnosis and treatment of prostate problems, prostate cancer, or other medical conditions during the study are charged to the participant in the same way as if he were not part of the trial. A participant's insurance will pay for diagnosis and treatment according to the plan's policies. If the participant has no insurance, social services may be available at the local level to cover costs for diagnosis and treatment.

**16. What other clinical trials are under way for prostate cancer prevention?**

In addition to SELECT, smaller trials are also being conducted with a variety of agents, including a vitamin D analog; soy isoflavones; and lycopene (a plant pigment common in tomatoes).

**17. Where is more information about SELECT available?**

In the United States and Puerto Rico, call the National Cancer Institute's Cancer Information Service at 1-800-4-CANCER (1-800-422-6237) for information in English or Spanish. People with TTY equipment can call 1-800-332-8615 for information in English. In Canada, call the Canadian Cancer Society's Cancer Information Service at 1-888-939-3333 for information in English or French.

The following Web sites provide additional information:

- <http://www.swog.org>—choose the SELECT option
- <http://www.cancer.gov/clinicaltrials/digestpage/SELECT>—from the NCI
- <http://www.cancer.gov/newscenter/SELECT>—provides images of the prostate, the crystalline and chemical structures of vitamin E, and selenium and vitamin E capsules

## Selected References

1. American Cancer Society (2005). *Cancer Facts and Figures 2005*. Atlanta, GA: American Cancer Society. Retrieved May 24, 2005, from <http://www.cancer.org/downloads/STT/CAFF2005f4PWSecured.pdf>.
2. Clark LC, Combs GF Jr., Turnbull BW, et al. Effects of selenium supplementation for cancer prevention in patients with carcinoma of the skin. A randomized controlled trial. Nutritional Prevention of Cancer Study Group. *Journal of the American Medical Association* 1996; 276(24):1957–1963.
3. Duffield-Lillico AJ, Reid ME, Turnbull BW, et al. Baseline characteristics and the effect of selenium supplementation on cancer incidence in a randomized clinical trial: A summary report of the Nutritional Prevention of Cancer Trial. *Cancer Epidemiology, Biomarkers & Prevention* 2002; 11(7):630–639.
4. Heinonen OP, Albanes D, Virtamo J, et al. Prostate cancer and supplementation with alpha-tocopherol and beta-carotene: Incidence and mortality in a controlled trial. *Journal of the National Cancer Institute* 1998; 90(6):440–446.
5. Duffield-Lillico AJ, Slate EH, Reid ME, et al. Selenium supplementation and secondary prevention of nonmelanoma skin cancer in a randomized trial. *Journal of the National Cancer Institute* 2003; 95(19):1477–1481.
6. Lonn E, Bosch J, Yusuf S, et al. Effects of long-term vitamin E supplementation on cardiovascular events and cancer: A randomized controlled trial. *Journal of the American Medical Association* 2005; 293(11):1338–1347.
7. Miller ER III, Pastor-Barriuso R, Dalal D, et al. Meta-analysis: High-dosage vitamin E supplementation may increase all-cause mortality. *Annals of Internal Medicine* 2005; 142(1):37–46.

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## Related Resources

### **Publications (available at <http://www.cancer.gov/publications>)**

- National Cancer Institute Fact Sheet 5.23, *Early Prostate Cancer: Questions and Answers*
- National Cancer Institute Fact Sheet 5.29, *The Prostate-Specific Antigen (PSA) Test: Questions and Answers*
- *Taking Part in Clinical Trials: Cancer Prevention Studies: What Participants Need To Know*
- *Understanding Prostate Changes: A Health Guide for All Men*
- *What You Need To Know About™ Prostate Cancer*

## **National Cancer Institute (NCI) Resources**

### **Cancer Information Service (toll-free)**

Telephone: 1-800-4-CANCER (1-800-422-6237)

TTY: 1-800-332-8615

### **Online**

NCI's Web site: <http://www.cancer.gov>

*LiveHelp*, NCI's live online assistance:

<https://cissecure.nci.nih.gov/livehelp/welcome.asp>

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