

Antioxidants and cancer

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- [Free radicals](#) are highly reactive chemicals that have the potential to harm cells. They are created when an atom or a molecule (a chemical that has two or more atoms) either gains or loses an electron (a small negatively charged particle found in atoms).
- Free radicals are formed naturally in the body and play an important role in many normal cellular processes. At high concentrations, however, free radicals can be hazardous to the body and damage all major components of cells, including DNA, proteins, and cell membranes. The damage to cells caused by free radicals, especially the damage to DNA, may play a role in the development of cancer and other health conditions

- The production of abnormally high levels of free radicals is the mechanism by which ionizing radiation kills cells. Moreover, some environmental toxins, such as cigarette smoke, some metals, and high-oxygen atmospheres, may contain large amounts of free radicals or stimulate the body's cells to produce more free radicals.

- [Antioxidants](#) are chemicals that interact with and neutralize [free radicals](#), thus preventing them from causing damage. Antioxidants are also known as “free radical scavengers.”
- The body makes some of the antioxidants that it uses to neutralize free radicals. These antioxidants are called [endogenous](#) antioxidants. However, the body relies on external (exogenous) sources, primarily the diet, to obtain the rest of the antioxidants it needs.
- These exogenous antioxidants are commonly called dietary antioxidants. Fruits, vegetables, and grains are rich sources of dietary antioxidants. Some dietary antioxidants are also available as [dietary supplements](#)

- Examples of dietary antioxidants include [beta-carotene](#), [lycopene](#), and vitamins A, C, and E ([alpha-tocopherol](#)).

The mineral element [selenium](#) is often thought to be a dietary antioxidant, but the antioxidant effects of selenium are most likely due to the antioxidant activity of proteins that have this element as an essential component (i.e., selenium-containing proteins), and not to selenium itself

- **Can antioxidant supplements help prevent cancer?**
- In laboratory and [animal studies](#), the presence of increased levels of exogenous [antioxidants](#) has been shown to prevent the types of [free radical](#) damage that have been associated with cancer development. Therefore, researchers have investigated whether taking dietary antioxidant [supplements](#) can help lower the risk of developing or dying from cancer in humans.
- Many [observational studies](#), including [case–control studies](#) and [cohort studies](#), have been conducted to investigate whether the use of dietary antioxidant supplements is associated with reduced risks of cancer in humans. Overall, these studies have yielded mixed results ([5](#)). Because observational studies cannot adequately control for biases that might influence study outcomes, the results of any individual observational study must be viewed with caution.

- Randomized [controlled clinical trials](#), however, lack most of the biases that limit the reliability of observational studies. Therefore, randomized trials are considered to provide the strongest and most reliable evidence of the benefit and/or harm of a health-related intervention. To date, nine randomized controlled trials of dietary antioxidant supplements for cancer prevention have been conducted worldwide. Many of the trials were sponsored by the National Cancer Institute. The results of these nine trials are summarized below.

Trial name, country (reference)	Intervention	Study subjects	Results
Linxian General Population Nutrition Intervention Trial, China (6, 7)	15 milligrams (mg) beta-carotene, 30 mg alpha-tocopherol, and 50 micrograms (µg) selenium daily for 5 years	Healthy men and women at increased risk of developing esophageal cancer and gastric cancer	Initial: no effect on risk of developing either cancer; decreased risk of dying from gastric cancer only Later: no effect on risk of dying from gastric cancer Later: no effect on risk of dying from gastric cancer
Alpha-Tocopherol/Beta-Carotene Cancer Prevention Study (ATBC), Finland (8–12)	Alpha-tocopherol (50 mg per day) and/or beta-carotene (20 mg per day) supplements for 5 to 8 years	Middle-aged male smokers	Initial: increased incidence of lung cancer for those who took beta-carotene supplements Later: no effect of either supplement on incidence of urothelial, pancreatic, colorectal, renal cell, or upper aerodigestive tract cancers

Carotene and Retinol Efficacy Trial (CARET), United States (13–15)

Daily supplementation with 15 mg beta-carotene and 25,000 International Units (IU) retinol

People at high risk of lung cancer because of a history of smoking or exposure to asbestos

Initial: increased risk of lung cancer and increased death from all causes—trial ended early

Later: higher risks of lung cancer and all-cause mortality persisted; no effect on risk of prostate cancer

Physicians' Health Study I (PHS I), United States (16)

Beta-carotene supplementation (50 mg every other day for 12 years)

Male physicians

No effect on cancer incidence, cancer mortality, or all-cause mortality in either smokers or non-smokers

Women's Health Study (WHS), United States (17, 18)

Beta-carotene supplementation (50 mg every other day), vitamin E supplementation (600 IU every other day), and aspirin (100 mg every other day)

Women ages 45 and older

Initial: no benefit or harm associated with 2 years of beta-carotene supplementation
Later: no benefit or harm associated with 2 years of vitamin E supplementation

Supplémentation en Vitamines et Minéraux Antioxydants (SU.VI.MAX) Study, France (19–22)

Daily supplementation with vitamin C (120 mg), vitamin E (30 mg), beta-carotene (6 mg), and the minerals selenium (100 µg) and zinc (20 mg) for a median of 7.5 years

Men and women

Initial: lower total cancer and prostate cancer incidence and all-cause mortality among men only; increased incidence of skin cancer among women only

Later: no evidence of protective

			Later: no evidence of protective effects in men or harmful effects in women within 5 years of ending supplementation
Heart Outcomes Prevention Evaluation—The Ongoing Outcomes (HOPE-TOO) Study, International (23)	Daily supplementation with alpha-tocopherol (400 IU) for a median of 7 years	People diagnosed with cardiovascular disease or diabetes	No effect on cancer incidence, death from cancer, or the incidence of major cardiovascular events
Selenium and Vitamin E Cancer Prevention Trial (SELECT), United States (24, 25)	Daily supplementation with selenium (200 µg), vitamin E (400 IU), or both	Men ages 50 and older	Initial: no reduction in incidence of prostate or other cancers—trial stopped early Later: more prostate cancer cases among those who took vitamin E alone
Physicians' Health Study II (PHS II), United States (26)	400 IU vitamin E every other day, 500 mg vitamin C every day, or a combination of the two	Male physicians ages 50 years and older	No reduction in incidence of prostate cancer or other cancers

- Overall, these nine randomized controlled clinical trials did not provide evidence that dietary antioxidant supplements are beneficial in primary cancer prevention. In addition, a systematic review of the available evidence regarding the use of vitamin and mineral supplements for the prevention of chronic diseases, including cancer, conducted for the United States Preventive Services Task Force (USPSTF) likewise found no clear evidence of benefit in preventing cancer

- It is possible that the lack of benefit in clinical studies can be explained by differences in the effects of the tested antioxidants when they are consumed as purified chemicals as opposed to when they are consumed in foods, which contain complex mixtures of antioxidants, vitamins, and minerals .
- Therefore, acquiring a more complete understanding of the antioxidant content of individual foods, how the various antioxidants and other substances in foods interact with one another, and factors that influence the uptake and distribution of food-derived antioxidants in the body are active areas of ongoing cancer prevention research.

- **You should talk with your doctor if you take antioxidant supplements or are thinking about trying one.** Supplements haven't been shown to protect against cancer, and they have the potential to interact with other medications you might be taking or have a negative impact on cancer treatment.
- recommend getting your antioxidants from food sources and avoiding supplements



THANK YOU!