

Vitamin D and Cancer Prevention

What is vitamin D?

Vitamin D is the name given to a group of fat-soluble prohormones (substances that usually have little hormonal activity by themselves but that the body can turn into hormones). Vitamin D helps the body use calcium and phosphorus to make strong bones and teeth. Skin exposed to sunshine can make vitamin D, and vitamin D can also be obtained from certain foods. Vitamin D deficiency can cause a weakening of the bones that is called rickets in children and osteomalacia in adults.

Two major forms of vitamin D that are important to humans are vitamin D₂, or ergocalciferol, and vitamin D₃, or cholecalciferol. Vitamin D₂ is made naturally by plants, and vitamin D₃ is made naturally by the body when skin is exposed to ultraviolet radiation in sunlight. Both forms are converted to 25-hydroxyvitamin D in the liver. 25-Hydroxyvitamin D then travels through the blood to the kidneys, where it is further modified to 1,25-dihydroxyvitamin D, or calcitriol, the active form of vitamin D in the body. The most accurate method of evaluating a person's vitamin D status is to measure the level of 25-hydroxyvitamin D in the blood.

Most people get at least some of the vitamin D they need through sunlight exposure. Dietary sources include a few foods that naturally contain vitamin D, such as fatty fish, fish liver oil, and eggs. However, most dietary vitamin D comes from foods fortified with vitamin D, such as milk, juices, and breakfast cereals. Vitamin D can also be obtained through dietary supplements.

The Institute of Medicine (IOM) of the National Academies has developed the following recommended daily intakes of vitamin D, assuming minimal sun exposure (1,2):

- For those between 1 and 70 years of age, including women who are pregnant or lactating, the recommended dietary allowance (RDA) is 15 micrograms (µg) per day. Because 1 µg is equal to 40 International Units (IU), this RDA can also be expressed as 600 IU per day.
- For those 71 years or older, the RDA is 20 µg per day (800 IU per day).
- For infants, the IOM could not determine an RDA due to a lack of data. However, the IOM set an Adequate Intake level of 10 µg per day (400 IU per day), which should provide sufficient vitamin D.

Although the average dietary intakes of vitamin D in the United States are below guideline levels, data from the National Health and Nutrition Examination Survey revealed that more than 80 percent of Americans had adequate vitamin D levels in their blood (2).

Even though most people are unlikely to have high vitamin D intakes, it is important to remember that excessive intake of any nutrient, including vitamin D, can cause toxic effects. Too much vitamin D can be harmful because it increases calcium levels, which can lead to calcinosis (the deposit of calcium salts in soft tissues, such as the kidneys, heart, or lungs) and hypercalcemia (high blood levels of calcium). The safe upper intake level of vitamin D for adults and children older than 8 years of age is 100 µg per day (4000 IU per day). Toxicity from too much vitamin D is more likely to occur from high intakes of dietary supplements than from high intakes of foods that contain vitamin D. Excessive sun exposure does not cause vitamin D toxicity. However, the IOM states that people should not try to increase vitamin D production by increasing their exposure to sunlight because this will also increase their risk of skin cancer (2).

Why are cancer researchers studying a possible connection between vitamin D and cancer risk?

Early epidemiologic research showed that incidence and death rates for certain cancers were lower among individuals living in southern latitudes, where levels of sunlight exposure are relatively high, than among those living at northern latitudes. Because exposure to ultraviolet light from sunlight leads to the production of vitamin D, researchers hypothesized that variation in vitamin D levels might account for this association. However, additional research based on stronger study designs is required to determine whether higher vitamin D levels are related to lower cancer incidence or death rates.

Experimental evidence has also suggested a possible association between vitamin D and cancer risk. In studies of cancer cells and of tumors in mice, vitamin D has been found to have several activities that might slow or prevent the development of cancer, including promoting cellular differentiation, decreasing cancer cell growth, stimulating cell death (apoptosis), and reducing tumor blood vessel formation (angiogenesis) (3-6).

What is the evidence that vitamin D can help reduce the risk of cancer in people?

A number of epidemiologic studies have investigated whether people with higher vitamin D intakes or higher blood levels of vitamin D have lower risks of specific cancers. The results of these studies have been inconsistent, possibly because of the challenges in carrying out such studies. For example, dietary studies do not account for vitamin D made in the skin from sunlight exposure, and the level of vitamin D measured in the blood at a single point in time (as in most studies) may not reflect a person's true vitamin D status. Also, it is possible that people with higher vitamin D intakes or blood levels are more likely to have other healthy behaviors. It may be one of these other behaviors, rather than vitamin D intake, that influences cancer risk.

Several randomized trials of vitamin D intake have been carried out, but these were designed to assess bone health or other non-cancer outcomes. Although some of these trials have yielded information on cancer incidence and mortality, the results need to be confirmed by additional research because the trials were not designed to study cancer specifically.

The cancers for which the most human data are available are colorectal, breast, prostate, and pancreatic cancer. Numerous epidemiologic studies have shown that higher intake or blood levels of vitamin D are associated with a reduced risk of colorectal cancer (7-10). In contrast, the Women's Health Initiative randomized trial found that healthy women who took vitamin D and calcium supplements for an average of 7 years did not have a reduced incidence of colorectal cancer (11). Some scientists have pointed out that the relatively low level of vitamin D supplementation (10 µg, or 400 IU, once a day), the ability of participants to take additional vitamin D on their own, and the short duration of participant follow-up in this trial might explain why no reduction in colorectal cancer risk was found. Evidence on the association between vitamin D and the risks of all other malignancies studied is inconclusive.

How is vitamin D being studied now in clinical cancer research?

Taken together, the available data are not comprehensive enough to establish whether taking vitamin D can prevent cancer (12). To fully understand the effects of vitamin D on cancer and other health outcomes, new randomized trials need to be conducted (13). However, the appropriate dose of vitamin D to use in such trials is still not clear (14). Other remaining questions include when to start taking vitamin D, and for how long, to potentially see a benefit.

To begin addressing these issues, researchers are conducting two phase I trials to determine what dose of vitamin D may be useful for chemoprevention of prostate, colorectal, and lung cancers (trial descriptions [here](#) and [here](#)). In addition, larger randomized trials have been initiated to examine the potential role of vitamin D in the prevention of cancer. The [Vitamin D/Calcium Polyp Prevention Study](#), which has finished recruiting approximately 2,200 participants, is testing whether vitamin D supplements, given alone or with calcium, can prevent the development of colorectal adenomas (precancerous growths) in patients who previously had an adenoma removed. The study's estimated completion date is December 2017. The Vitamin D and Omega-3 Trial ([VITAL](#)) will examine whether vitamin D supplements can prevent the development of a variety of cancer types in healthy older men and women ([15](#)). The organizers of VITAL expect to recruit 20,000 participants and complete the trial by June 2016.

Researchers are also beginning to study vitamin D analogs--chemicals with structures similar to that of vitamin D--which may have the anticancer activity of vitamin D but not its ability to increase calcium levels ([16](#)).

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