

For the Public: What the AREDS Means for You

What the Age-Related Eye Disease Studies Mean for You

Researchers with the Age-Related Eye Disease Study (AREDS) reported in 2001 that a nutritional supplement called the AREDS formulation can reduce the risk of developing advanced age-related macular degeneration (AMD). The original AREDS formulation contains vitamin C, vitamin E, beta-carotene, zinc and copper.

In 2006, the same research group, which is based at NIH's National Eye Institute, began a second study called AREDS2 to determine if they could improve the AREDS formulation. They tested...

- Adding the antioxidants lutein and zeaxanthin
- Adding omega-3 fatty acids
- Removing beta-carotene
- Lowering the dose of zinc

This page provides information about the results and implications of AREDS2. If you are at risk for advanced AMD or have a family member who is at risk, the questions and answers below may help you discuss using AREDS and related nutritional supplements with a health care professional.

What is the original AREDS formulation?

- 500 milligrams (mg) of vitamin C
- 400 international units of vitamin E
- 15 mg beta-carotene
- 80 mg zinc as zinc oxide
- 2 mg copper as cupric oxide

What modifications were tested in AREDS2?

- 10 mg lutein and 2 mg zeaxanthin
- 1000 mg of omega-3 fatty acids (350 mg DHA and 650 mg EPA)
- No beta-carotene
- 25 mg zinc

Why change the formulation?

Why add lutein/zeaxanthin and omega-3 fatty acids? Previous studies had found that dietary intake of lutein/zeaxanthin and omega-3 fatty acids is associated with a lower risk of developing advanced AMD.

Why eliminate beta-carotene? During the AREDS trial, two large trials funded by the National Cancer Institute found that beta-carotene may increase lung cancer risk among people who smoke. Lutein and zeaxanthin are in the same family of nutrients as beta-carotene and are believed to have

important functions in the retina. Therefore, the researchers theorized that lutein/zeaxanthin might be a safer and possibly more effective alternative than beta-carotene.

Why reduce zinc? Although zinc was found to be an essential component of the AREDS formulation in the original trial, some nutritional experts recommended a lower dose.

What formulation should I take?

Consult your doctor or eye care professional about which supplement, if any, is right for you. The ingredients based on AREDS and AREDS2 research are:

- 500 milligrams (mg) of vitamin C
- 400 international units of vitamin E
- 80 mg zinc as zinc oxide
- 2 mg copper as cupric oxide
- 10 mg lutein and 2 mg zeaxanthin

What are lutein, zeaxanthin and beta-carotene?

Lutein, zeaxanthin, and beta-carotene belong to a family of nutrients known as carotenoids. Carotenoids are made by plants and are especially enriched in green leafy vegetables. They can be stored in animal tissues and are found at relatively low levels in animal food products. In the body, beta-carotene is used to make Vitamin A, which is required by the retina to detect light and convert it into electrical signals. Beta-carotene itself is not found in the eye. In contrast, lutein and zeaxanthin are found in the retina and lens, where they may act as natural antioxidants and help absorb damaging, high-energy blue and ultraviolet light.

What are omega-3 fatty acids?

Omega-3 fatty acids are made by marine algae and enriched in fish oils; they are believed to be responsible for the health benefits associated with regularly eating fish, including lower rates of cardiovascular disease. The AREDS2 study focused on the omega-3 fatty acids DHA and its precursor EPA. DHA is needed for the integrity of the retinal cells, and has been shown to promote retinal development and repair in prior studies.

What were the effects of changing the original AREDS formulation?

In the first AREDS trial, taking the original formulation reduced the risk of advanced AMD by about 25 percent over a five-year period. In the AREDS2 trial, adding DHA/EPA or lutein/zeaxanthin to the original formulation (containing beta-carotene) had no additional overall effect on the risk of advanced AMD. However, trial participants who took AREDS containing lutein/zeaxanthin and no beta-carotene had a slight reduction in risk of advanced AMD, compared with those who took AREDS with beta-carotene. Also, for participants with very low levels of lutein/zeaxanthin in their diet, adding these supplements to the AREDS formulation helped lower their risk of advanced AMD. Finally, former smokers who took AREDS with beta-carotene had a higher incidence of lung cancer. (Please see below for more details on the effects of lutein/zeaxanthin vs. beta-carotene.) The investigators found no significant changes in the effectiveness of the formulation when they removed beta-carotene or lowered zinc.

Who should consider taking a combination of antioxidants and zinc like those examined in AREDS and AREDS2?

People at high risk for developing advanced AMD should consider taking the antioxidant-zinc combinations examined in AREDS and AREDS2. These people are defined as having either:

1. Intermediate AMD in one or both eyes. Intermediate AMD can be detected by an eye care professional, but usually involves little or no vision loss.
2. Advanced AMD in one eye, but not the other eye. Advanced AMD involves either a breakdown of cells in the retina (called geographic atrophy or dry AMD), or the growth of abnormal blood vessels under the retina (called neovascular or wet AMD). Either of these forms of advanced AMD can cause vision loss.

Will taking an AREDS formulation prevent AMD?

There is no known treatment that can prevent the early stages of AMD. However, the AREDS formulations may delay progression of advanced AMD and help you keep your vision longer if you have intermediate AMD, or advanced AMD in one eye. The participants in the first AREDS trial have now been followed for 10 years, and the benefits of the AREDS formulation have persisted over this time.

Can I take a daily multivitamin if I am taking one of the AREDS formulations?

Yes. The AREDS formulation is not a substitute for a multivitamin. In the AREDS trial, two-thirds of the study participants took multivitamins along with the AREDS formulation. In AREDS2, almost nine of ten participants took multivitamins.

Can a daily multivitamin alone provide the same vision benefits as an AREDS formulation?

No. The vitamins and minerals tested in the AREDS and AREDS2 trials were provided in much higher doses than what is found in multivitamins. Also, it is important to remember that most of the trial participants took multivitamins. Taking an AREDS formulation clearly provided a benefit over and above multivitamins.

Can diet alone provide the same high levels of antioxidants and zinc as the AREDS formulations?

No. The high levels of vitamins and minerals are difficult to achieve from diet alone. However, previous studies have suggested that people who have diets rich in green, leafy vegetables—a good source of lutein/zeaxanthin—have a lower risk of developing AMD. In the AREDS2 trial, the people who seemed to benefit most from taking lutein/zeaxanthin were those who did not get much of these nutrients in their diet. Within this group, those who received lutein/zeaxanthin supplements had a 26

percent reduced risk of developing advanced AMD compared with those who did not receive the supplements.

What is the risk of lung cancer from taking beta-carotene?

In the AREDS2 trial, current smokers or those who had quit smoking less than a year before enrollment were excluded from receiving beta-carotene. Despite this precaution, lung cancers were observed in 2 percent of participants who took an AREDS formulation with beta-carotene, compared with 0.9 percent of participants who took AREDS without beta-carotene. Across both groups, about 91 percent of participants who developed lung cancer were former smokers.

Are Former Smokers at an Increased Risk for Developing Lung Cancer if They Take High Doses of Beta-Carotene?

Large clinical trials sponsored by the National Cancer Institute demonstrated that beta-carotene increases the risk of lung cancer in current smokers. In these trials, most of these smokers were heavy smokers. The only other large clinical trial evaluating beta-carotene was the Physicians Health Study (PHS). In the PHS, there was no evidence of increased cancer risk in those randomly assigned to beta-carotene, but few physicians were active smokers. There also was no evidence of an increased risk of lung cancer in former smokers. However, many studies suggest that former smokers maintain some increased risk of lung cancer for years after stopping smoking. Therefore, it is reasonable to expect that beta-carotene may also slightly increase their risk of cancer, at least for a period of several years.

In deciding whether to include beta-carotene in a formulation designed to slow the development of advanced AMD, you and your doctor should balance the apparent increase in the risk of lung cancer associated with beta-carotene with the risk of AMD progression.

How does lutein/zeaxanthin compare to beta-carotene?

Lutein/zeaxanthin has not been associated with increased cancer risk. Moreover, analysis from the AREDS2 trial suggests that it offers similar or better protective benefits against advanced AMD, compared with beta-carotene. In the trial, participants who took an AREDS formulation containing lutein/zeaxanthin (no beta-carotene) had an 18 percent lower risk of progressing to advanced AMD compared with those who took AREDS containing beta-carotene (no lutein/zeaxanthin).

Does the high-dose vitamin E in the AREDS formulations affect the risk of prostate cancer?

There have been conflicting data on the relationship between vitamin E and prostate cancer.

- In 1994, the Alpha-Tocopherol, Beta Carotene (ATBC) trial found a 35 percent *reduced* risk of prostate cancer in men taking 50 mg of vitamin E daily for a follow-up of six years.

- In 2009, the Physicians Health Study II (PHS II) found that 400 IU of vitamin E every other day for a follow-up of eight years had *no effect* on the incidence of prostate cancer.
- In 2011, the Selenium and Vitamin E Cancer Prevention Trial (SELECT) found a 17 percent *increase* in the risk of prostate cancer among men taking 400 IU of vitamin E daily for a follow-up of seven years. That risk equates to 1-2 more prostate cancers per 1000 patients who took high-dose vitamin E for one year. For reasons that are unclear, men who took both vitamin E and selenium did not have an increased rate of prostate cancer.

In the AREDS trial, high-dose vitamin E had no effect on the risk of prostate cancer among male participants. The AREDS2 trial began in 2006 (before the SELECT trial was reported) and all study participants were offered an AREDS formulation containing vitamin E. A group of independent researchers monitoring the AREDS2 trial for safety noted no concerns about an increased risk prostate cancer. The final data from the study do not suggest a higher rate of prostate cancer among male participants than expected in an aging male population.

If you have concerns about vitamin E and prostate cancer, it is important to understand that many factors influence the risk of prostate cancer, including age, family history and race. Visit the National Cancer Institute web site for [more information about prostate cancer risk factors\(link is external\)](#), and talk to your health care provider about the possible risks and benefits from taking vitamin E supplements.

Are there any other side effects or risks from taking the AREDS formulations?

Many older Americans take prescription medications, and a considerable number use over-the-counter drugs, dietary supplements, and herbal medicines. High-dose supplemental nutrients can sometimes interfere with medications and compete with other vital nutrients for absorption into the body. Individuals who are considering taking an AREDS formulation should discuss this with their primary care doctors and/or eye care professionals.

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