

Results from the Age-Related Eye Disease Study



A R E D S

Age-Related Eye Disease Study

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The Effect of Antioxidant Vitamins and Zinc Mineral Supplements on Age-related Macular Degeneration and Cataract

The Age-Related Eye Disease Study (AREDS) has helped us learn more about macular degeneration and cataract, two leading causes of vision loss in older adults. This study included a clinical trial to test whether taking antioxidants could help prevent or slow the progression of cataract, and whether these antioxidants and zinc could help prevent or slow the progression of age-related macular degeneration (AMD).

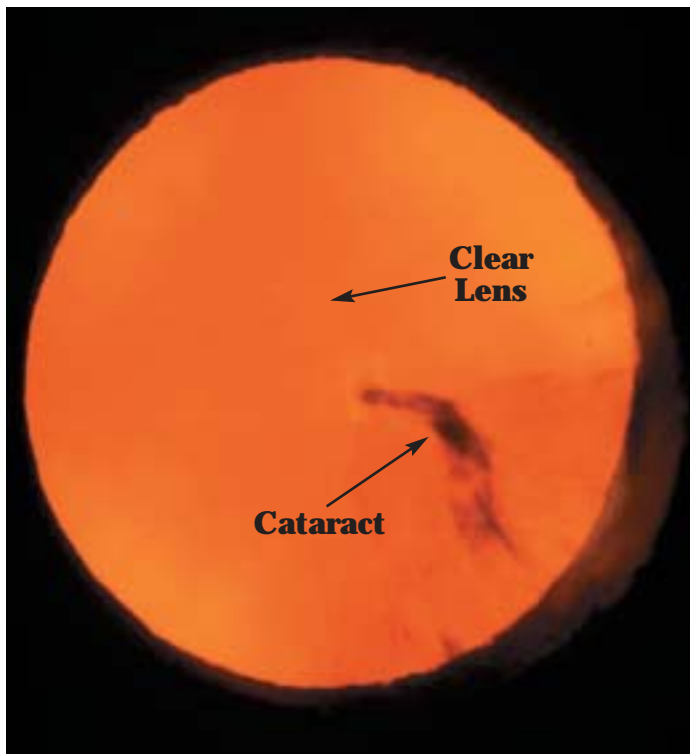
The National Eye Institute, part of the Federal Government's National

Institutes of Health, sponsored the study. Enrollment in AREDS began in November 1992. Nationwide, 4,757 participants enrolled in the study at eleven clinical centers and were assigned randomly (meaning that the treatment was selected by chance) to take either the antioxidant tablets only; zinc tablets only; tablets containing both antioxidants and zinc; or a placebo (a harmless substance).

This booklet will explain the results of this study.

What is a cataract?

A *cataract* is a clouding in the normally clear *lens* of the eye. As a cataract develops, vision may become hazy, fuzzy, or blurry. The eye may become more sensitive to light or glare, and people often notice that they need more light to read. During the study, participants had regular photographs taken of the lens. These photos were used to document development or progression of cataract. This is a photograph of one type of cataract.



CATARACT

What is age-related macular degeneration?

Age-related macular degeneration (AMD) affects the part of the eye called the macula, which is the part of the eye's inner lining called the retina. The macula is the tiny, central part of the retina that we use for sharp, straight-ahead vision such as reading, driving, and recognizing faces of friends. AMD is a leading cause of visual impairment and legal blindness in Americans 65 years of age or older.

A common feature found in people with AMD are tiny yellow spots beneath the retina called drusen. Many people over age 60 have at least a few small drusen, although some people have none at all and some people have large or extensive drusen. Participants entering AREDS were categorized into groups based on the number and size of the drusen present in their eyes and whether they had any advanced signs of AMD. Advanced signs of AMD are leakage or bleeding in the eye (the advanced "wet" form of macular degeneration), or a loss of light sensitive cells and supporting tissue in the central retinal area (the advanced "dry" form of macular degeneration). Both of these problems cause significant central vision loss. Photographs of the retina were used to assign participants to a category and identify eyes that progressed to advanced AMD during the study.

It is important to understand how participants were categorized because the recommendations from this study are different for people with different eye characteristics. The categories are as follows:

Category 1
No AMD

No drusen or a few small drusen

Category 2
Early AMD

Several small drusen or a few medium-sized drusen, in one or both eyes

Category 3
Intermediate AMD

Many medium-sized drusen or one or more large drusen, in one or both eyes

Category 4
Advanced AMD

In one eye only:

Either a loss of light-sensitive cells and supporting tissue in the central retinal area (dry form), or abnormal and fragile blood vessels under the retina (wet form)

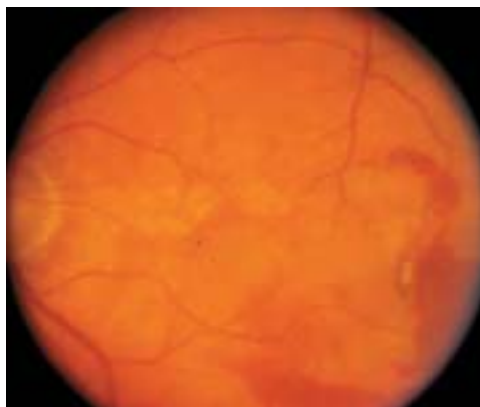
These are examples of eye photographs from someone without any AMD, with intermediate AMD, and with the advanced “wet” form of AMD:



No AMD



Intermediate AMD



Advanced “wet” AMD

TREATMENTS

AREDS randomly assigned participants to one of four treatment groups. Participants received daily oral tablets of either: 1) zinc alone; 2) antioxidants alone; 3) a combination of antioxidants and zinc; or 4) a placebo, a harmless substance that looks like the real treatment but has no active ingredients. The antioxidant formulation contained a combination of vitamin C, vitamin E, and beta-carotene. The specific daily amounts of antioxidants and zinc used by the AREDS researchers were 500 milligrams of vitamin C; 400 International Units of vitamin E; 15 milligrams of beta-carotene; 80 milligrams of zinc in the form of zinc oxide; and two milligrams of copper in the form of cupric oxide. In the study's planning stages, a panel of nutritionists, ophthalmologists, and biochemists reviewed the scientific and epidemiological data and recommended these vitamins and dosages.

At the beginning of the study, the AREDS investigators believed that people who had no drusen or only a few drusen in their eyes (Category 1) would not have a high risk of developing advanced AMD changes during the study. Therefore, these participants were assigned to take either antioxidant alone or a placebo tablet. They were not given tablets with zinc.

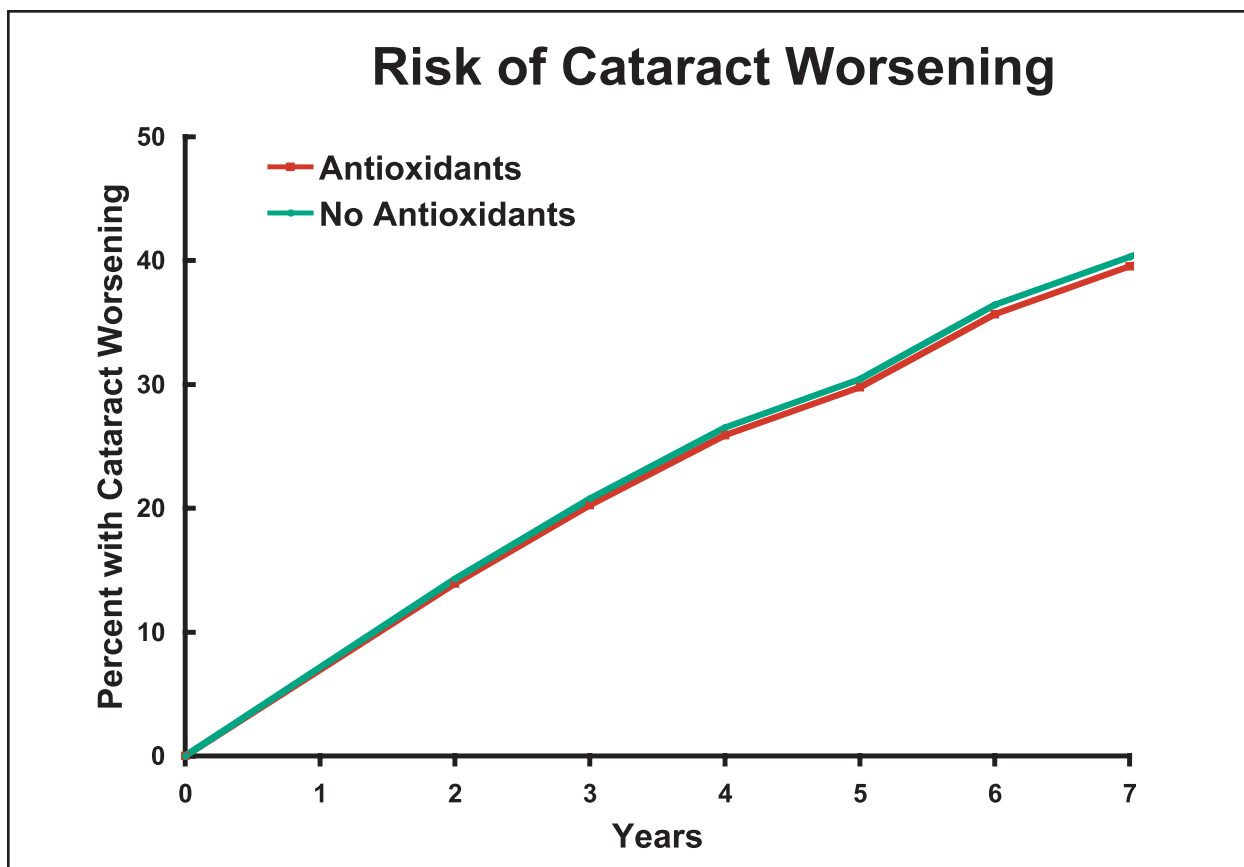
RESULTS

Cataract

After an average treatment time of 6.3 years, the AREDS vitamin and mineral tablets had *no apparent effect* on the development or progression of cataract or on the rate of having cataract surgery.

Participants taking tablets with antioxidants were about as likely to develop cataracts as those who took tablets without antioxidants. No tablet — including those containing zinc — seemed to have an effect on vision change due to cataract. The graph shows the percent of people whose cataract worsened during the study by treatment assignment.

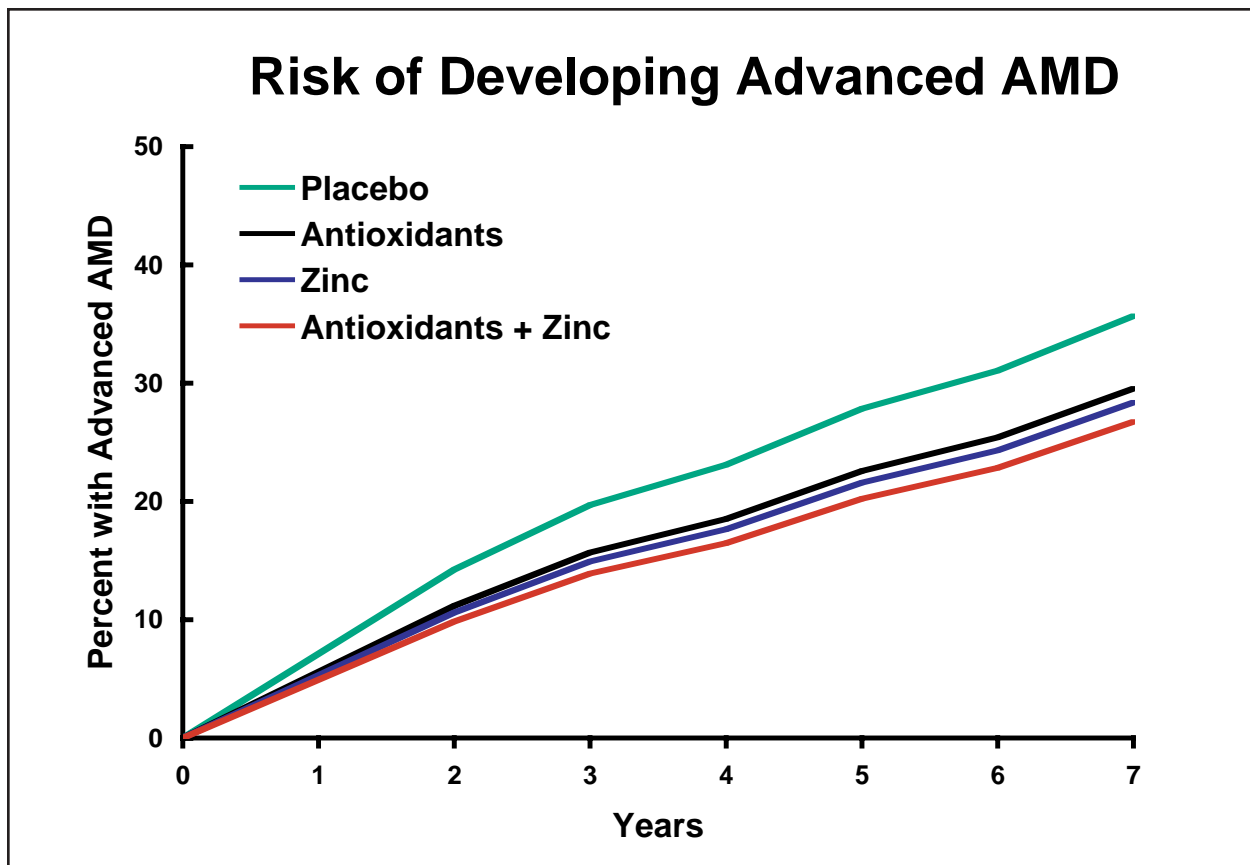
At this time, the AREDS investigators do not feel that the vitamin and mineral supplements in AREDS containing the study ingredients (vitamins C and E, beta-carotene, and/or zinc) will help slow cataract development or vision loss from cataracts. However, the investigators cannot tell from this study whether these antioxidants taken for a longer time or whether taking different antioxidants might slow the progression of cataract.



Age-related Macular Degeneration

For those study participants who initially had early AMD (Category 2), less than two percent developed advanced AMD over five years. Without treatment, those with intermediate AMD had an 18 percent chance of developing advanced AMD in one or both eyes over 5 years, and those with advanced AMD in only one eye had a 43 percent chance of developing advanced AMD in the other eye. AREDS scientists found that

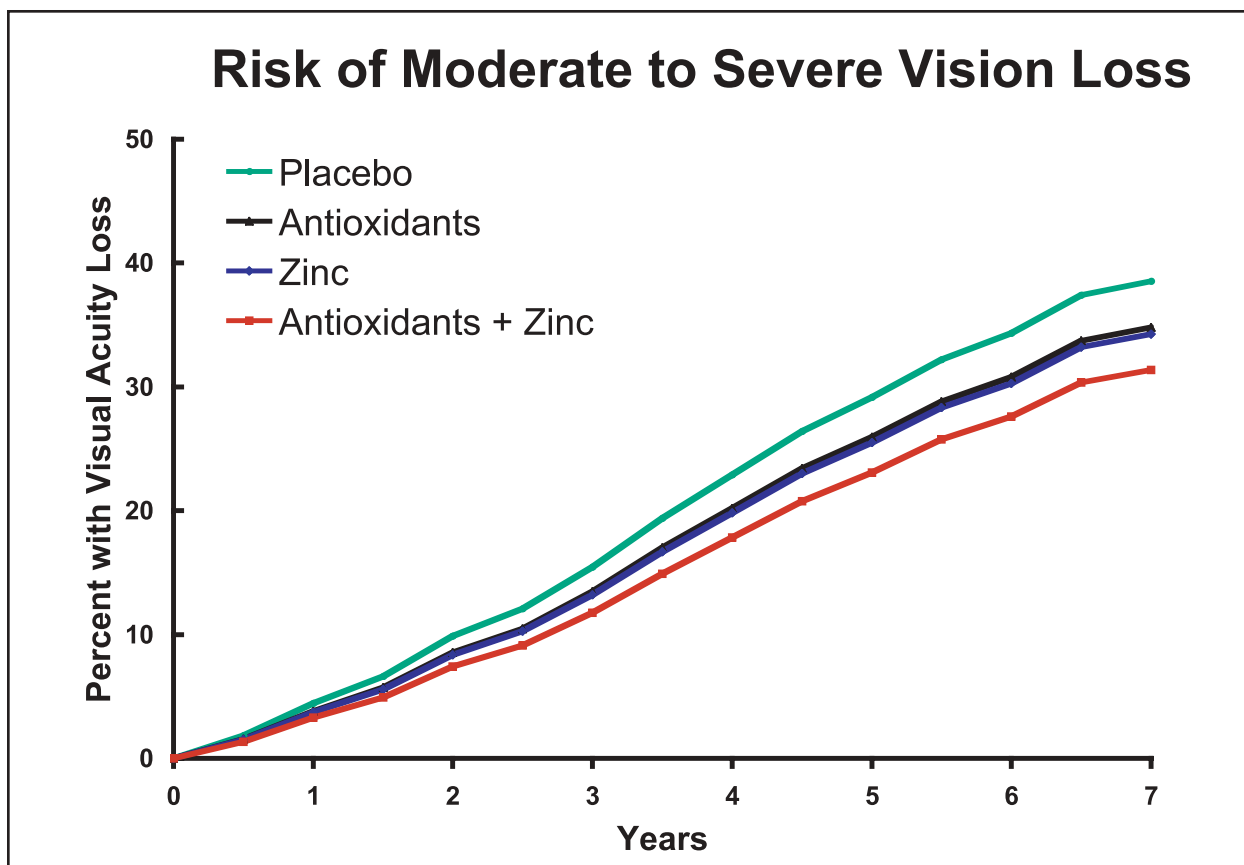
people at high risk for developing advanced stages of AMD — that is people with intermediate AMD or advanced AMD in one eye — lowered their risk by about 25 percent when treated with the tablets containing "antioxidants plus zinc" compared to placebo. The graph shows the percent of people who developed advanced AMD during the study by treatment assignment.



In the same high-risk group — which includes people with intermediate AMD or with advanced AMD in one eye but not the other eye — the "antioxidant plus zinc" tablets reduced the risk of moderate or severe vision loss by about 19 percent.

This is an exciting discovery because it means that the "antioxidant plus zinc" tablets are the first effective treatment to *slow the progression* of AMD and/or vision loss for people who are at high risk for developing advanced AMD. The graph shows the percent of people losing 15 letters or more (3 or more lines) of vision on the vision chart by treatment assignment.

Participants at high risk for developing advanced AMD who took the "zinc alone" tablets reduced this risk by about 21 percent and their risk of vision loss by about 11 percent. Participants who were treated with the "antioxidants alone" tablets reduced their risk of developing advanced stages of AMD by about 17 percent and their risk of vision loss by about 10 percent.



The chart below summarizes the results for AMD and vision loss:

Antioxidants Plus Zinc

- Reduced risk of developing advanced AMD by about 25 percent
- Reduced risk of vision loss by about 19 percent

Zinc Alone

- Reduced risk of developing advanced AMD by about 21 percent
- Reduced risk of vision loss by about 11 percent

Antioxidants Alone

- Reduced risk of developing advanced AMD by about 17 percent
- Reduced risk of vision loss by about 10 percent

There is no apparent need for those diagnosed with early AMD to take the supplements studied in AREDS. AREDS researchers found that the “antioxidants plus zinc” did not slow the disease’s progression from early AMD to intermediate AMD. However, those with early AMD should have dilated eye examinations every year to determine if the disease has progressed to the intermediate stage.

The study was not designed to evaluate the effect of the supplements in study participants who initially had no AMD (Category 1). This is because previous studies had indicated that people aged 60 and over with no AMD have a very low risk for developing a clear progression of AMD. The Age-Related Eye Disease Study confirmed this low risk — participants with no AMD had less than a one percent chance of losing vision from AMD during the study.

Side Effects

AREDS participants reported minor side effects from the treatments. About 7.5 percent of participants assigned to the zinc treatments — compared with 5 percent who did not have zinc in their assigned treatment — had urinary tract problems that required hospitalization. Participants in the two groups that took zinc also reported anemia at a slightly higher rate (13 percent) than people not taking zinc (10 percent); however, testing of all patients for this disorder showed

no difference among treatment groups. Participants taking antioxidants reported yellowing of the skin, a well-known side effect of large doses of beta-carotene, slightly more often. Beta-carotene has been shown in two other studies to increase the risk of death in people who smoke. People who smoke should discuss with their primary care doctor and/or eye care specialist whether or not they should take supplements like those used in AREDS.

Summary

People who are at high risk for developing advanced AMD should consider taking supplements like those used in AREDS. These high-risk people have either:

1. **Intermediate AMD in one or both eyes.** Intermediate AMD is defined as the presence of either many medium-sized drusen or one or more large drusen.

or

2. **Advanced AMD in one eye, but not the other eye.** Advanced AMD is defined as either a loss of light-sensitive cells and supporting tissue in the central retinal area (advanced "dry" form), or the development of abnormal and fragile blood vessels under the retina (advanced "wet" form) that can leak fluid or bleed. Either of these forms of advanced AMD can cause vision loss.

Your eye care professional can tell you if you have AMD — and its level of development — through an eye exam in which drops are placed in the eyes to dilate the pupils. This allows for a careful examination of the inside of the eye.

There is no apparent need for those diagnosed with early AMD to take the supplements studied in AREDS. This study did not demonstrate that the supplements provided a benefit to those with early AMD. Many people with early AMD progressed to intermediate AMD during the study, and the AREDS supplements did not seem to slow this progression. However, if you have early AMD, a dilated eye examination every year can help determine whether the disease is progressing.

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