



## AGE-RELATED EYE DISEASE STUDY AREDS Coordinating Center

Dear AREDS Participant,

A paper to be published in the January 2005 edition of the *Annals of Internal Medicine* will report that taking high-dose vitamin E supplements does not lower the risk of death, and might be associated with a small increase in the risk of death. The material in this paper was recently presented at a meeting of the American College of Physicians in New Orleans and this presentation has received much attention from the press. The authors conducted an analysis looking at the risk of death by combining data from 19 clinical trials testing vitamin E as a possible treatment for many different diseases. Results from the Age-Related Eye Disease Study (AREDS) were included in the analysis. We are writing to tell you about the results of this report and why we believe taking 400 International Units (IU) of vitamin E as part of the AREDS formulation does not increase the risk of death of persons at risk for advanced AMD.

In this new study, the authors concluded that, “high-dosage ( $\geq 400$  IU) vitamin E supplements may increase all-cause mortality.” Their data does seem to show that persons taking particularly high doses of vitamin E (500 IU to 2000 IU) may have some increased risk of death, but even at the high doses, the risks observed for patients ranged from a benefit of 2% to a risk of 5%, with most of the studies having an excess risk between 0.5% and 4%. In addition, it is not clear that this possible increased risk for very high doses would apply to persons taking 400 IU. This is important to our study participants because this is the dose of vitamin E in the AREDS formulation. Looking at all the studies included in this new analysis of vitamin E, there are three studies, including AREDS, that evaluated about 400 IU of vitamin E daily (two 400 IU and one 440 IU). There were over 15,000 patients followed in these three studies and over 1600 total deaths in this generally elderly population. In total, the group taking the vitamin E was actually just slightly more likely to be living after 5 years (801 deaths out of 7564 persons in the vitamin E group and 806 deaths out of 7598 in the placebo group). This means there was essentially no difference in the risk of dying between those who took about 400 IU vitamin E and those who did not in a large number of patients studied.

If the reason for taking vitamin E is to decrease mortality, we agree with the authors of this new study that there does not seem to be any benefit of vitamin E for most patients and there might be some harm at high doses. However, as you know, if you are at high risk for developing advanced age-related macular degeneration (AMD), there is a benefit in taking the AREDS formulation that includes vitamin E. AREDS data show that you can reduce the risk of developing advanced AMD by about 25%. The AREDS data also indicate that the antioxidants in the formulation were partly responsible for that benefit. This means the possible benefit of vitamin E should be considered when deciding whether to take the AREDS formulation.

The AREDS formulation contains a number of antioxidants and minerals other than just vitamin E. We also looked at the risk of death in AREDS for those who were taking the AREDS formulation compared with those who were assigned to the placebo group. Those taking the AREDS formulation actually had a 12% reduction in 5-year mortality risk. Although this reduction in mortality risk was not statistically significant, and we cannot say that the formulation will improve your longevity, it does suggest that taking the AREDS supplement is unlikely to increase your risk of dying.

Because different patients have different needs, it is important to discuss with your doctor whether this formulation is right for you.