

From The JAMA Network

Food Antioxidants to Prevent Cataract

Julie Mares, PhD

JAMA OPHTHALMOLOGY

Total Antioxidant Capacity of the Diet and Risk of Age-Related Cataract: A Population-Based Prospective Cohort of Women

Susanne Rautiainen, PhD; Birgitta Ejderik Lindblad, MD, PhD;
Ralf Morgenstern, PhD; Alicja Wolk, DMSc

IMPORTANCE To our knowledge, no previous epidemiologic study has investigated the association between all antioxidants in the diet and age-related cataract. The total antioxidant capacity (TAC) concept aims to measure the capacity from all antioxidants in the diet by also taking synergistic effects into account.

OBJECTIVE To investigate the association between the TAC of the diet and the incidence of age-related cataract in a population-based prospective cohort of middle-aged and elderly women.

DESIGN, SETTING, AND PARTICIPANTS Questionnaire-based nutrition survey within the prospective Swedish Mammography Cohort study, which included 30 607 women (aged 49-83 years) who were observed for age-related cataract incidence for a mean of 7.7 years.

EXPOSURE The TAC of the diet was estimated using a database of foods analyzed with the oxygen radical absorbance capacity assay.

MAIN OUTCOMES AND MEASURES Information on incident age-related cataract diagnosis and extraction was collected through linkage to registers in the study area.

RESULTS There were 4309 incident cases of age-related cataracts during the mean 7.7 years of follow-up (234 371 person-years). The multivariable rate ratio in the highest quintile of the TAC of the diet compared with the lowest was 0.87 (95% CI, 0.79-0.96; *P* for trend = .03). The main contributors to dietary TAC in the study population were fruit and vegetables (44.3%), whole grains (17.0%), and coffee (15.1%).

CONCLUSIONS AND RELEVANCE Dietary TAC was inversely associated with the risk of age-related cataract. Future studies examining all antioxidants in the diet in relation to age-related cataract are needed to confirm or refute our findings.

JAMA Ophthalmol. 2014;132(3):247-252.
doi:10.1001/jamaophthalmol.2013.6241.

Cataract is the leading cause of blindness and visual impairment worldwide. In developing countries, the relatively simple, low-cost surgical excision of cataract is not widely available, and the social burden is high. In developed countries, cataract surgery is available; more than half of people aged 80 years and older in the United States have had cataract surgery.¹ Cataract surgery and related medical costs in the United States are estimated to be \$6.8 billion per year² and are likely to increase because of increasing rates of cataract surgery and the aging of the population. Lens opacities, which develop before surgery is indicated, can make seeing more difficult, especially under dim light and under conditions of glare, such as when driving at night.

Most lens opacities develop slowly over a lifetime. If preventive measures could delay cataract development by 10 years, the visual and surgical burden of this disease might be reduced by 50%.³ Cataracts are caused by oxidative stress and osmotic imbalances resulting from the accumulated stresses of physiological and environmental factors, combined with reduction in the eye's ability to defend against, or repair, the damage. Ultraviolet light exposure, smoking, diabetes, and excessive alcohol use are all associated with cataract formation, and these conditions are also associated with greater oxidative stress.

The biological mechanisms protecting against oxidative stress are complex and involve many interacting chemicals. These include some vitamins, such as vitamins C and E, which can directly quench free radicals and reduce and regenerate antioxidants; some essential minerals, such as zinc, selenium, and manganese, are cofactors for enzymes that catalyze reactions that lower oxidative stress. However, these chemicals also include lesser studied, nonnutritive food components, such as lutein and flavonoids, which have antioxidant properties. The prospective cohort study by Rautiainen and colleagues⁴ reported in *JAMA Ophthalmology* was the first to evaluate the incidence of cataract extraction surgery in relation to an estimate of a person's dietary total antioxidant capacity (TAC). This study, in the Swedish Mammography cohort, assessed the TAC of a person's diet using a previously described and validated food frequency questionnaire and food TAC database that reflects the levels of, and synergism between, many known and unknown antioxidant compounds in foods, based on the oxygen radical absorbance capacity assay. The TAC value for each food reflects the content of antioxidants such as vitamins C, vitamin E, and beta-carotene, which have been common components of high-dose antioxidant supplements, despite a lack of evidence of benefit in lowering cataract risk.⁵ A food's TAC also reflects many other less well-studied

nonnutritive antioxidants. The major food contributors to the TAC of participants' diets included fruits and vegetables, whole grains, and coffee. Rautiainen et al⁴ reported a modest but significant protective association with total dietary antioxidants: 1 SD difference in TAC level (equivalent to the daily intake of 1-2 apples or 2 peppers) lowered risk for getting cataract surgery by 1% to 6% over an 8-year time span.

The lens preferentially accumulates some antioxidant nutrients, such as lutein, zeaxanthin, vitamin E, and vitamin C, but not others, like beta-carotene. The degree to which other nonnutritive antioxidant compounds in foods enter the lens is unknown. However, food antioxidant compounds could lower cataract risk by decreasing systemic turnover of lutein and zeaxanthin or other antioxidant nutrients that do enter the lens. Consistent with this possibility, in a separate study by the same investigators,⁶ urinary markers for systemic oxidative stress were directly related to cataract risk.

Could supplements take the place of consuming antioxidant-rich foods? A newly published study of US physicians was the second randomized, double-blind, placebo-controlled clinical trial of more than 9 years in length to observe that multivitamins containing several essential antioxidant nutrients lowered risk for cataract, especially for nuclear cataract.⁷ Over 11.2 years, multivitamin use lowered risk 9% (hazard ratio, 0.91; 95% CI, 0.83-0.99). However, multivitamins may have provided benefit for reasons other than their antioxidant content. Also, multivitamins do not provide all antioxidants present in foods.

An example of antioxidants in foods that might benefit the eye in particular are the carotenoids lutein and zeaxanthin. These are preferentially taken up by the lens and other eye tissues (like the macula) and are being actively studied for their potential benefits. They are not yet considered essential nutrients and have not been included in most multivitamin supplements. Although their intake is associated with lower cataract risk in prospective studies, there is insufficient evidence that these results specifically reflect the benefit of lutein and zeaxanthin, rather than merely act as markers for antioxidant-rich vegetable and fruit intake. In a recently completed randomized, double-blind, placebo-controlled trial over 5 years in people with age-related macular degeneration, lower cataract development rates were observed in participants having the lowest dietary levels of lutein and zeaxanthin,⁸ when moderate levels of lutein and zeaxanthin were added to a supplement containing other high-dose antioxidants. However, these results were from secondary analyses; the primary analyses indicated no reduced cata-

ract incidence over the 5-year period of the study. Also, little is known about the long-term benefits and risks of lutein taken in supplements; it is an active area of investigation.

Although there is a lack of consistent evidence that supplements containing higher doses of a single antioxidant or combinations of antioxidants lower cataract risk,⁵ some observational studies suggest possible harm. In fact, in 2 separate 8-year, prospective cohort studies of Swedish men and women,^{9,10} high doses of supplemental vitamins C and E were associated with greater cataract risk. Vitamin C supplement use was associated with an increased risk of cataract extraction in women. In men, the use of vitamin C- or vitamin E-containing supplements increased the risk of cataract extraction or diagnosis. These risks were stronger in older patients and higher in persons with other cataract risk factors: corticosteroid use in both men and women and hormone replacement therapy in women. The possibility cannot be ruled out that persons who use vitamin C- and vitamin E-containing supplements have unknown or unmeasured risk factors for cataract that in part explain these results. However, these study results must be considered together with a larger body of evidence suggesting mechanisms for harmful effects. Antioxidants can also function as pro-oxidants, increasing oxidative stress in the lens under certain conditions. Moreover, antioxidants may have deleterious effects elsewhere in the body. An increasing but poorly understood body of evidence suggests that oxygen radicals have some beneficial roles, which large doses of supplemental antioxidants may hamper.

What is the clinical and public health message that can be made from the current body of evidence about antioxidant-rich food and supplements in relation to slowing the development of cataracts? Healthy, plant-rich diets are associated with lower cataract risk. The study by Rautiainen et al⁴ in *JAMA Ophthalmology* adds to that evidence. Moderate levels of antioxidant supplements, such as those provided by many multivitamins, have benefit in lowering risk for some types of cataract but lack antioxidant constituents in foods, which might have added benefit. High-dose antioxidant supplements might be medically important for lowering progression of certain eye diseases, such as macular degeneration, but may not lower the risk of cataract in people consuming healthy diets and may increase risk at high doses. Further studies are needed to better understand the relationship between food-derived antioxidants and cataract prevention. In the meantime, eat vegetables and fruits.

ARTICLE INFORMATION

Author Affiliation: Department of Ophthalmology and Visual Sciences, University of Wisconsin, Madison.

Corresponding Author: Julie Mares, PhD, Department of Ophthalmology and Visual Sciences, University of Wisconsin, 610 N Walnut St, 1063 WARF Bldg, Madison, WI 53726-2336 (jmarespe@wisc.edu).

Conflict of Interest Disclosures: The author has completed and submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest and none were reported.

REFERENCES

- Congdon N, Vingerling JR, Klein BE, et al. Prevalence of cataract and pseudophakia/aphakia among adults in the United States. *Arch Ophthalmol*. 2004;122(4):487-494.
- Vision Problems in the US. <http://www.visionproblemsus.org/ataract/ataract-definition.html>. Accessed May 23, 2014.
- Kupfer C. Bowman lecture: the conquest of cataract. *Trans Ophthalmol Soc U K*. 1985;104(pt 1):1-10.
- Rautiainen S, Lindblad BE, Morgenstern R, Wolk A. Total antioxidant capacity of the diet and risk of age-related cataract. *JAMA Ophthalmol*. 2014;132(3):247-252.
- Mathew MC, Ervin AM, Tao J, Davis RM. Antioxidant vitamin supplementation for preventing and slowing the progression of age-related cataract. *Cochrane Database Syst Rev*. 2012;6:CD004567.
- Selin JZ, Lindblad BE, Rautiainen S, et al. Are increased levels of systemic oxidative stress and inflammation associated with age-related cataract? *Antioxid Redox Signal*. 2014;21(5):700-704.
- Christen WG, Glynn RJ, Manson JE, et al. Effects of multivitamin supplement on cataract and age-related macular degeneration in a randomized trial of male physicians. *Ophthalmology*. 2014;121(2):525-534.
- Chew EY, SanGiovanni JP, Ferris FL, et al. Lutein/zeaxanthin for the treatment of age-related cataract. *JAMA Ophthalmol*. 2013;131(7):843-850.
- Rautiainen S, Lindblad BE, Morgenstern R, Wolk A. Vitamin C supplements and the risk of age-related cataract. *Am J Clin Nutr*. 2010;91(2):487-493.
- Zheng Selin J, Rautiainen S, Lindblad BE, Morgenstern R, Wolk A. High-dose supplements of vitamins C and E, low-dose multivitamins, and the risk of age-related cataract. *Am J Epidemiol*. 2013;177(6):548-555.