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Healthy Diets and the Subsequent Prevalence of Nuclear Cataract in Women

Julie A. Mares, PhD, Rick Volland, PhD, Rachel Adler, BS, RD, Lesley Tinker, PhD, AE Millen, PhD, Suzen M. Moeller, PhD, Barbara Blodi, MD, Karen M. Gehrs, MD, Robert B. Wallace, MD, Richard J. Chappell, PhD, Marian L. Neuhouser, M., PhD, G Sarto, MD, PhD, and the CAREDS Study Group

Department of Ophthalmology and Visual Sciences (Drs Moeller, Volland, Blodi, Adler and Mares), the Department of Statistics and Biostatistics (Dr. Chappell), Gloria E. Sarto, M.D., Ph.D. and the Department of Obstetrics and Gynecology, Center for Women's Health Research, University of Wisconsin, Madison, WI ; Division of Public Health Sciences, Fred Hutchinson Cancer Research Center, Seattle, WA (Drs. Tinker and Neuhouser); the Department of Social and Preventive Medicine, University at Buffalo, Buffalo, NY (Dr. Millen); University of Iowa Hospital & Clinics (Dr. Gehrs); and the Department of Epidemiology, University of Iowa, Iowa City, IA (Dr. Wallace)

Abstract

Objective and Design—The association between healthy diet scores which reflect adherence to the US Dietary Guidelines and prevalence of nuclear cataract, assessed four to seven years later, was assessed in a sample of Women's Health Initiative (WHI) Observational Study participants (50–79 years of age) who were residing in Iowa, Wisconsin and Oregon. Scores on the 1995 Healthy Eating Index (HEI-95), which reflect adherence to 1990 guidelines, were assigned from responses to food frequency questionnaires at WHI-baseline (1994–1998). Presence of nuclear cataract was determined from slit-lamp photographs and self-report of cataract extractions were assessed from 2001–04 in the Carotenoids in Age-Related Eye Disease Study (N=1,808).

Results—Having a high HEI-95 score was the strongest modifiable predictor of low prevalence of nuclear cataract among numerous risk factors investigated in this sample. The multivariable-adjusted OR and 95% confidence interval for high vs. low quintile for diet score were 0.6 (0.4–0.9). Higher prevalence of nuclear cataract was also associated with other modifiable factors (smoking and marked obesity) and non-modifiable factors (having brown eyes, myopia and high pulse pressure). Vitamin supplement use was not related to cataract.

Conclusion—These data add to the body of evidence suggesting that eating foods that are rich in a variety of vitamins and minerals, may contribute to postponing the occurrence of the most common type of cataract in the US.

INTRODUCTION

Cataracts, which increase in prevalence with age, are the most important cause of blindness in the world.¹ In the US, cataract is the most prevalent cause of visual impairment due to eye disease² and surgery to remove lenses with cataracts accounts for approximately 60% of vision-related Medicare expenditures.³ The number of Americans affected by cataract and undergoing cataract surgery is expected to increase dramatically over the next 20 years as the US population ages.⁴ As more aging Americans need cataract surgery, there is concern about

To whom correspondence should be sent: Julie A. Mares, PhD Professor University of Wisconsin Department of Ophthalmology and Visual Sciences 610 N. Walnut Street; 1063 WARF Building Madison, Wisconsin 53726-2336 (608) 262-8044 FAX: (608) 265-9279 jmarespe@wisc.edu.

the ability of health care systems, particularly Medicare, to fund cataract surgeries.³ Therefore, identifying modifiable risk factors is of critical importance to improving health of older Americans and to the economic stability of the health care system.

Nuclear cataract is the most common type of cataract among older Americans⁵ and the most common type of cataract for which surgical extraction is performed.⁶ This type of cataract is frequently more common in women,^{4, 7, 8} people with brown eyes^{7, 8} and those who have myopia^{8, 9, 10} or diabetes^{8, 9, 11} and people with low education.⁷ Many modifiable risk factors have been suggested. Smoking is the most commonly and consistently reported modifiable risk factor in population studies (previously reviewed¹²). Others that are sometimes observed in population studies include having a higher^{13–15} or lower^{13, 16} body mass index, heavy use of alcoholic beverages^{17–19} and diets which are low in one or more nutrients or high in fat or refined carbohydrates.^{20–27, 28, 29, 30}

Several aspects of diet may lower risk for nuclear cataract by lowering oxidative stress or systemic inflammation (which can lead to oxidative stress). Having adequate or high intakes or blood levels of lutein and zeaxanthin^{20–27} and the use of multivitamin supplements (recently reviewed^{28, 29}) have been most consistently related to lower risk for cataract. Often, but less consistently, high diet or blood levels of vitamins C and/or E (recently reviewed³⁰ and subsequently reported^{21, 22, 31}) have been associated with lower risk. A few studies have also suggested many other aspects of diet associated with lower risk for nuclear cataract or cataract extraction including high intake of long chain³² or total³³ omega-3 fats or low intake of carbohydrate³⁴ or refined carbohydrates (as indicated by a low glycemic index score)³⁵ or overall fats³⁶ or certain types of fat³⁷. Only one previous study has directly evaluated the overall impact of a healthy diet on the occurrence of cataract. They observed that adherence to 1990 Dietary Guidelines for Americans, as reflected by Healthy Eating Index (HEI) scores for diets over a ten year time period, was associated with lower risk for early nuclear lens opacities.³⁸

The Carotenoids in Age-Related Eye Disease Study (CAREDS), an ancillary study of the Women's Health Initiative (WHI),³⁹ was designed, in part, to evaluate the relationships of the carotenoids lutein and zeaxanthin to the prevalence of age-related nuclear cataract and age-related macular degeneration. We previously reported that high dietary and blood levels of lutein and zeaxanthin were associated with lowered risk for nuclear cataract in this cohort.³⁶ There are limited studies published to date in which nutritional risk factors are evaluated concurrently with a comprehensive set of other lifestyle, ocular health and physical risk factors. The availability of extensive risk factor data from the WHI and CAREDS investigations permits the description of the relationships of overall diet patterns, use of supplements and an extensive set of other potential risk factors related to low prevalence of nuclear cataract in the present report.

METHODS

Study Sample

The WHI Observational Study³⁹ is a prospective cohort study of the most common causes of mortality and morbidity among 93,676 postmenopausal women 50 to 79 years of age at enrollment, at 40 sites around the United States. The original cohort was recruited to the WHI at each of these sites through regional mass-mailings and mass-media strategies, from among women ineligible for or uninterested in participation in the WHI Clinical Trials. Participants were followed on average 7 years after enrollment. Women were excluded if they had medical conditions that predicted survival of less than three years, alcoholism, drug dependency, or mental illness.^{40, 41}

The CAREDS population consists of women who were enrolled in the observational study of the WHI at 3 of 40 sites: the University of Wisconsin (Madison), the University of Iowa (Iowa City), and the Kaiser Center for Health Research (Portland), who had self-reported intakes of lutein plus zeaxanthin that were either above the 78th or below the 28th percentiles, as assessed at baseline enrollment into the WHI in 1994–1998, as previously described.³⁶ Of 3,143 women who fulfilled these criteria and formed the recruitment pool, 96 died or were lost to follow-up between sample selection in year 2000 and enrollment in the CAREDS in 2001–2004. Those remaining were sent letters inviting them to participate in the CAREDS. A total of 1,042 women declined participation and 2,005 were enrolled (64%). Of those enrolled, we excluded women from the present analyses for the following reasons: WHI found that diet data was unreliable (n=1), history of trauma to both eyes (n=32), reported cataract extraction before the age of 40y (n=1), missing or upgradeable nuclear lens photographs (n=132) and participants who were missing covariate data (n=31). Thus, 1,808 women comprised the analysis dataset for this investigation. All procedures conformed to the Declaration of Helsinki and were approved by the Institutional Review Board at each University.

Nutritional estimates—Estimates of daily food and nutrient intake were made from responses to a previously validated, semi-quantitative food frequency questionnaire (FFQ)⁴² at WHI baseline (1994–98). Adherence to the 1990 Dietary Guidelines for Americans and 1992 Food Guide Pyramid, reflecting dietary recommendations at the time that women entered the WHI, was estimated by Healthy Eating Index (HEI)-1995 scores⁴³ adapted to this questionnaire, as previously described.⁴⁴ The HEI-1995 score includes 10 components, each with a possible score range of 0–10. A summary of score components is given in Table 1. For the food group components (grains, vegetables, fruits, milk, meat), scores were based upon intake of the recommended servings of each food group for women over 55 years of age. Scores between 0 and 10 were given proportionally according to the frequency with which the participant reported eating each food, compared to the Dietary Guidelines recommended number of servings. For total fat, energy intake of 30% or less from fat was given the maximum score of 10 and intake of 45% or more of energy from fat was given a score of 0. For saturated fat, intake of less than 10% of energy from saturated fat was given a 10 and intake of 15% or more of energy from saturated fat was given a 0. For cholesterol, intake less than 300 mg/day was given a 10; whereas intake of greater or equal to 450 mg/day was given a 0. Sodium intake less than 2400 mg/day was given a 10, and sodium intake greater than or equal to 4800 mg/day was given a 0. For variety, at least 16 different food items over three days was given a score of 10; whereas intake of 6 or fewer different types of food over three days was given a 0.

The Dietary Guidelines for Americans and the Food Guide Pyramid were updated in 2005.⁴⁵ Therefore, we also explored relationships of nuclear cataract to estimated adherence to these more recent guidelines using the HEI-2005 score, developed by Guenther, et al.⁴⁶ Briefly, the HEI-2005 score includes 12 components, with maximum component scores ranging from 5–20 per component and a maximum total composite score of 100. A summary of score components is given in Table 1. The component scores were based on nutrient density values rather than on absolute levels of foods eaten, using energy estimates for women over age 55 year. They also reflect guidance about specific foods to consume within larger food groups. For example, the 2005 guidelines recommend, in addition to 5–9 serving of fruits and vegetables/day, to specifically eat dark green leafy vegetables, dark orange vegetables and legumes several times per week. The 10 points devoted to the vegetable score included 5 points for total servings of vegetable and 5 points for the specific servings of dark green or orange vegetables. In addition, points for fat intake were assigned differently. The recommendation for fat intake was between 20 to 35% of energy, with most fats coming from sources of polyunsaturated and monounsaturated fats, such as fish, nut and vegetable oils. Thus, points

were given for low intake of saturated fat (<7% of energy) and low energy from solid fat, sugars and alcohol and for high intake of oils (≥ 12 g/1000 kcal) of oils.

Supplement use was queried at WHI baseline (1994–98). In addition, detailed data on the frequency and duration of multivitamins and high dose antioxidants were queried in questionnaires submitted at the CAREDS study visit (2001–2004). Use of high dose antioxidants at CAREDS baseline were defined as daily intake of at least 2 of the following 3 antioxidant supplements containing ≥ 120 mg vitamin C, ≥ 60 IU (40mg) vitamin E, and $\geq 10,000$ mcg beta-carotene. Women using these supplements for less than two years before the time photographs were taken were compared with women using supplements for greater than two years, (2–5 years, 5–10 years and more than 10 years).

Serum samples were obtained from participants at WHI baseline examinations (1994–1998) after a ≥ 12 -hour fast and were stored at -80 degrees C.³⁹ Serum levels of lutein, zeaxanthin, and tocopherols were determined at Tufts University (2004–2005) by reverse-phase HPLC .
47

Age-Related Nuclear Cataract—Lens photography and eye examinations were part of the CAREDS study visits that took place between 2001–2004 using the standardized Early Treatment for Diabetic Retinopathy Study protocol⁴⁸ modified as in the Age-Related Eye Disease Study, for which grading reliability has been previously reported.⁴⁹ Briefly, both eyes were examined with slit lamp biomicroscopy. After pharmacological dilation of the pupils, a single nonstereoscopic photograph was taken of each eye with a modified Topcon slit lamp camera to grade nuclear sclerosis and nuclear color using the Age-Related Eye Disease Study (AREDS) protocol.⁵⁰ Optical density of nuclear opacity was graded against a series of seven standard photographs producing continuous scores on a decimal scale that can range from 0.9 to 7.1. Severity of nuclear sclerosis was determined in eyes that had not previously undergone cataract extraction. Dates of cataract extraction in each eye, trauma to eyes, and physician diagnosed histories of cataract, glaucoma and macular degeneration and treatments and lifestyle changes that accompanied these conditions were queried in questionnaires collected at the time of lens photography.

The primary outcome was the presence of nuclear cataract, defined as a nuclear sclerosis severity score of 4 or greater in the worst eye and/or a history of cataract extraction in either eye. It was previously determined, in a similar population, that the incidence of cataract surgery was highest among people with photographically evident cataracts in the nuclear region of the lens⁶, suggesting that nuclear cataracts in women who had received cataract extractions were likely. Nuclear sclerosis, defined as a severity score ≥ 4 was a secondary outcome among women who had at least one natural lens for which lens photographs were gradable (1,577 women were eligible for this outcome).

Non-Nutritional Covariates—The following were queried at the CAREDS study visit: age, family history of cataract (immediate family member under age 75 years when diagnosed) and ultraviolet B (UV-B) sunlight exposure (since age 18 years and in last 20 years) based on outdoor activities during weekday, weekend and vacation periods, living location, and use of protective gear [hats or sunglasses] and time on water). Iris color was classified from photographs and refractive error from examination at the CAREDS eye exam. Additional demographic, lifestyle, and health history data were available from questionnaires completed at WHI study entry (education, smoking, physical activity, height, weight, hormone replacement therapy use, alcohol use, pulse pressure, and history of diabetes, hypertension, and cardiovascular disease). Histories of smoking, alcohol use and diabetes were updated at CAREDS study visits.

Statistical analyses—Odds ratios (ORs) and 95 percent confidence intervals (CIs) for nuclear cataract and for nuclear sclerosis scores ≥ 4 (yes/no) were calculated by exposure categories in models adjusted for age (continuous variable) using logistic regression (PROC LOGISTIC in SAS v.9.1, SAS Institute, Cary, NC). A multivariate cataract risk factor model was constructed including age and all risk factors that could biologically cause cataracts if they were related ($p < 0.10$) to either nuclear sclerosis or nuclear cataract in univariate analyses. The strongest OR was entered first and other covariates were re entered until no other covariates fell into the model at $p < 0.10$.

RESULTS

In this study sample, there was a wide range of intakes of many different foods: an approximately 3-fold or greater difference between the 10th and 90th percentile cut points for intakes of most individual food components that comprise HEI-95 scores. (Table 1) Women whose overall scores for HEI-95 were in the highest vs. lowest quintiles had diets that were lower in fat, saturated fat and sodium and higher in lutein and zeaxanthin, vitamin C and vitamin E (Table 2) and all other vitamins and minerals estimated (data not shown). Women with high 1995-HEI score levels were also more likely to be older and have schooling beyond high school. In addition, they were more likely to have characteristics which are often associated with Americans who adopt healthy lifestyles: being more likely to take supplements and less likely to smoke, more likely to have lower body fat (as reflected by BMI) and higher levels of physical activity. (Table 2)

Association of Nuclear Cataract with High Diet Quality

Nuclear cataract was common in this sample; present in 454 (29 %) of women who had lenses in at least one eye ($n=1577$). An additional 282 (16 % of 1808 women) had reported cataract extractions in either eye. Overall, 736 women (41%) had either nuclear cataracts, evident from lens photographs, or reported having a cataract extracted. The prevalence increased steeply with age; about 5-fold with each increasing decade. (Table 3)

Table 3 describes age-adjusted and multivariate-adjusted ORs and 95% CIs for nuclear cataract by healthy diet scores and other potential risk factors identified in Table 2. Because the risk factors were nearly identical for nuclear sclerosis defined in women with intact lenses and for nuclear cataract, including cataract extractions, ORs are given only for the latter and more common endpoint. Minor exceptions are noted in the text below.

The strongest modifiable risk factor in this sample was having a high overall diet quality score, as reflected by HEI-1995 score. After adjustment for other risk factors, being in the third to fifth quintiles for the HEI-1995 score, having HEI-1995 scores >68 , was associated with a 37% lower odds for nuclear cataract (Table 3). This was not influenced by further adjustment for energy which was unrelated to nuclear cataract (data not shown). Odds did not decrease linearly with increasing score; HEI-scores above quintile 3 did not further lower odds for nuclear cataract.

Having better diets, as reflected by higher HEI-1995 scores were associated with many other aspects of healthy lifestyle or potential protective factors for nuclear cataract. (Table 2) However, the association of HEI-1995 score with nuclear cataract did not appear to be completely explained by other measured aspects of healthy lifestyle, as it remained significant after adjusting for smoking and BMI (Table 3) and supplement use and physical activity (data not shown).

This association was also not driven by any single dimensions of diet. The prevalence of nuclear cataract was related to low values for most subscale scores (vegetables, fruits, milk, grains;

total fat saturated fat and variety; data not shown). Exceptions were for sub scores for meat intake which were directly related to nuclear cataract (not shown; p trend = 0.07) and for sub scores for sodium and cholesterol for which there was little variability and no relation to nuclear cataract (data not shown).

We conducted additional exploratory analyses in order to further consider which nutrients or single components of diet may have contributed to the overall inverse associations of HEI-95 score to nuclear cataracts. As previously described,⁵¹ levels of lutein and zeaxanthin in diet and in serum were inversely associated with nuclear cataract. HEI-1995 score is correlated with dietary lutein and zeaxanthin (Spearman's correlation coefficient = 0.4, $p < 0.0001$). Adjusting for lutein and zeaxanthin in the diet (Multivariate OR (95%CI) = 0.69 (0.97–1.02)) only slightly attenuated the association between HEI-1995 score and nuclear cataract, suggesting that higher intakes of these carotenoids only partly explained the associations between nuclear cataract and HEI-95 scores.

Women with higher HEI-1995 score had higher vitamin C intakes than those with lower scores (median of 169 vs. 67mg/day among women in high vs. low quintile for HEI-95 score). Further adjustment of the OR for nuclear cataract among women with high vs. low HEI-95 scores, for vitamin C intake from foods attenuated the ORs (Multivariate OR (95%CI) = 0.76 (0.50–1.15)), suggesting that higher vitamin C intakes partly explained the associations with HEI-95. However, there was a significant linear trend for a protective association of vitamin C intake from foods, but not from foods and supplements combined, even after multivariate adjustment including HEI-1995 score, suggesting the possibility of remaining protective associations of vitamin C containing foods, rather than vitamin C, itself.

The level of alpha-tocopherols (vitamin E) in foods, foods and supplements combined or serum was not significantly related to nuclear cataract (Table 2). Also, adjusting for vitamin E from foods did not alter the association of the HEI-1995 score to nuclear cataract (data not shown.)

We previously reported that the prevalence of nuclear cataract in this sample was associated with diets high in fat⁵¹ and speculated that this might reflect the possibility that dietary fat intake is a marker for diet that is poor in a wide variety of micronutrients. Indeed, dietary fat intake was highly correlated with HEI-1995 score ($r = 0.7$; $p < 0.0001$) and adjusting associations for dietary fat attenuated the odds ratio more than adjusting for any other nutrient (Multivariate OR (95%CI) = 0.86 (0.54–1.37)).

HEI-2005 Score

Nuclear cataract was not related to highest scores on a diet pattern that were intended to reflect adherence to more recent dietary guidelines (HEI-2005), even though the odds for nuclear cataract decreased with increasing quintile for HEI-2005 score from quintiles 2–4. (Table 3) We explored associations between nuclear cataract and subscale scores for HEI-2005 to understand the reason for the discrepancy between results for the two HEI scoring systems. Women in the highest quintile for HEI-2005 score had higher, rather than lower, intakes of oils (liquid oils, such as corn or canola oils) (median = 7.6 g/day) than women in the fourth quintile for HEI-2005 score (5.4 g/day) and the fifth quintile for HEI-95 score (4.5g/day). Oil intake above vs. below the median was associated with higher prevalence of nuclear cataract (adjusted odds ratio (95%CI) = 1.6(1.2–2.1). Furthermore, after excluding the oil sub score from the HEI-2005 index and recomputing HEI-2005 score, women in the highest vs. lowest quintile had lower odds for nuclear cataract: Multivariate (Table 3).

Estimate of Potential Impact of Healthy Diets

The potential impact of having healthy diets on age at which a visually significant cataract was present was estimated in the subsample of women who had at least one lens (1,577 women) by examining the linear fit line for the relationship between nuclear sclerosis score and age at photography among women with HEI-1995 scores above vs. below the 20th percentile cut point (59 points). (We omitted women <55 years at photography because their were too few cases of nuclear sclerosis >4 to make this comparison) The mean age at which visually significant nuclear cataract (nuclear sclerosis >4) was present was 2.9 years earlier for women with healthy diet scores greater vs. less than this cut point (76.4 vs 73.5 y), after adjusting for non-modifiable risk factors (iris color and pulse pressure). After further adjusting for non-dietary modifiable risk factors (BMI, smoking, physical activity) the mean age at which this level of severity was observed was slightly lowered to 2.4 years earlier (76.3 vs. 73.9 y). This relationship between diet and nuclear sclerosis score >4 was consistent across all ages and can be observed in the linearized curves (Figure) and in curves in which all data points were fit with spline curves (not shown). The slopes of the lines were not significantly different (p interaction=0.39), but a sample size of over 7,500 people would be required to detect an interaction with 90% power at $\alpha=0.05$.

Other Risk Factors

Risk factors for cataract have been previously evaluated in the absence of adjustment for broad health diet patterns and were, therefore, evaluated here, along with risk factors that have not been extensively studied (UV light exposure, and physical activity). Some risk factors were associated with the prevalence of nuclear cataract in this sample even after adjustment for having high scores on the HEI-1995. (Table 3) This included some directly modifiable risk factors (smoking and having a body mass index (BMI) > 35mm/kg²), pulse pressure and several non-modifiable risk factors (myopia and having dark brown eyes).

There were not clear associations with supplement use. The prevalence of nuclear cataract, including cataract extractions, was lower in women who used multivitamin supplements for more than two years prior to lens photographs, as compared to less than two years (OR(95% CI)= 0.82 (0.67–1.02), but the association was not significant, nor was it after multivariate adjustment. (Table 3) Moreover, the association did not strengthen with increasing duration of use: (Multivariate-adjusted OR (95% CI) = 1.05 (0.76–1.43), in 272 women who reported to consumed these supplements for more than ten years, compared with 896 women who reported taking supplements for less than 2 years prior to lens photography. Regular use of multivitamins at WHI baseline was also not related to nuclear cataract. (Multivariate OR (95% CI) = 0.96 (0.77–1.19) among the 874 women who regularly used multivitamins at WHI baseline, vs. compared with those who did not (934 women).

The use of high-dose antioxidant supplements was not related to nuclear cataract (Table 3). This remained true when comparing 160 women who had used such supplements for more than ten years with those who did not use high-dose antioxidants or had used them for <2 years before eye photographs were taken (Multivariate OR (95% CI) =1.16 (0.79–1.70).

Having a family history of cataracts before age 65 y was not associated with risk for nuclear cataract. Some risk factors for nuclear cataract that have been identified in other samples were not observed in the present study. These included, ocular exposure to UV-B light (Table 2) low education, history of arthritis, diabetes or asthma, hypertension, use of cholesterol lowering medication or hormone replacement therapy or heavy alcohol use (data not shown).

COMMENT

Results from the present study indicate that healthy diets, which reflect adherence to the US Dietary Guidelines at the time of entry in the WHI study, are more strongly related to the lower occurrence of nuclear cataracts than any other risk modifiable or protective factor studied in this sample of women. Being above the 20th percentile for scores that reflect adherence to US Dietary Guidelines in 1995, was associated with a 37% lower risk for nuclear cataract, after adjusting for other nondietary risk factors. The Healthy Eating Index was originally developed at the United States Department of Agriculture as an index of overall diet quality that incorporated the nutrient needs of healthy Americans and US Dietary Guidelines in 1990 for reduction of risk of major chronic diseases. [Kennedy, 1995 #50] These indices were based on scientific knowledge of relationships between diet and only the the major chronic diseases of cardiovascular diseases and cancer and did not address risk for eye diseases which were less well understood at that time. The results of the present study indicate that higher scores on this index also relate to reduced risk for the most common type of cataract in the United States.

The median HEI-1995 score for US women over 50 years of age in the National Health and Nutrition Examination Survey, conducted in close proximity in time to when the WHI baseline diets were assessed (1988–1994) was 64, as it was in this sample. These data suggest that eating diets which are “more nutritious than average” might be related to a similar magnitude in reduction in risk for nuclear cataract among American women. (However, this estimate in primarily Caucasian women may not approximate the impact in women of other ethnicities or men.)

It was previously estimated that a ten-year delay in the onset of cataracts could cut the number of cataract surgeries needed in half.⁵² We attempted to evaluate the impact of healthy diets on the age at which visually significant cataracts develop in an exploratory analyses using a subsample of the sample in the present study (Figure). We estimated that healthy diet, controlled for other healthy lifestyles, could be related to a 2.4 year delay in the presence of visually significant nuclear cataract. While this is the best available estimate, to date, it is likely to be an underestimate of the delay in cataracts that healthy diets might result in, for several reasons. First, these analyses use a subsample and have less statistical power than associations presented for the entire group of women in Table 3. Second, attenuation of risk estimates that occur by inevitable measurement error usually biases the association toward the null. This includes error due to imperfect measurement at entry into the WHI study, as well as error due to the estimation of diet over a shorter period of time than might influence the development of nuclear opacities. (Nuclear opacities are detected as early as the third decade of life in some people and may develop over many decades.) Third, the different intercepts in the Figure suggest the possibility that women with healthy diets had less severe opacities before this relationship was assessed in the present study. Fourth, some modifiable risk factors which were controlled for (BMI for example) likely reflect, to some extent, better diets at earlier ages. Also, in practice, improvements in one aspects of healthy lifestyles (such as being more physically active or stopping smoking) often accompany improvements in diet. There are only a few existing study samples which have photographic evidence of the severity of nuclear sclerosis, in which such estimates can be made. The impact of diet and healthy lifestyles on delaying cataracts and cataract surgeries might be better estimated from existing large, long-term prospective studies, particularly if data from these samples are pooled.

No further reduction in prevalence of nuclear cataract was associated with having HEI-1995 scores above 59 points (Table 1), even though it was associated with higher intakes of many nutrients that are thought to protect against cataract (Table 2), suggesting that once adequate levels of intake are attained, further increases may not be protective. However, some aspects of diet, such as reflected by a general trend for low prevalence of nuclear cataract with higher

intake of vitamin C intake from foods, remained associated with further reduced risk, suggesting that the HEI-1995 score may not have captured all protective aspects of foods.

These data confirm results in a separate sample of relatively healthy older women that indicated that HEI-95 scores above the median were associated with lower risk for nuclear cataracts.³⁸ “In both studies a design that is a hybrid between cross-sectional studies and prospective studies is used. That is, in both cases dietary data were assessed years before lens status was assessed (4 to 7 years in the present study and 9 to 11 years in the other study). This increases the likelihood of a temporally correct relationship. The fact that this endpoint is determined by photograph in the present study, rather than by diagnosis or self-report, strengthens the likelihood that the data reflect a temporal relationship (poor diet leads to nuclear cataract rather than the other way around). Finally, and importantly, the association between healthy diet patterns and nuclear cataract does not disappear or markedly weaken in younger women in the sample, as we would expect if poor diet occurred as a result of cataract or comorbid conditions. (The youngest women in this sample would have been less likely than older women to have had cataracts or other co-morbid conditions for many years prior to when diet was assessed) (data not shown in the entire cohort, but can be visualized for a subsample in the Figure)” However, prospective studies over a decade or more and studies which include men can provide more precise estimates of risk reduction in the general population that can be achieved with healthy diets.

The lack of association of nuclear cataract with HEI-2005 score does not necessarily suggest that adhering to the current (2005) US Dietary Guidelines are less protective against nuclear cataract and might reflect, instead, a limitation in the diet scoring system. After removing the score for high oil intake, similar results were obtained with either score. Although oil intake is recommended to achieve an adequate vitamin E intake and might be related to low risk for other chronic diseases, it was related to higher, rather than lower, risk for nuclear cataract in this sample. A separate scoring system that reflects adherence to the 2005 USDA Food Guide Pyramid has been developed.⁵³ It is not known whether scores using this alternative system are more strongly related to nuclear cataract risk. This is a newly developing field and improved ability to estimate diet quality may improve our ability to study the impact of diet on cataract.

These results did not appear to be influenced by other measures of a healthy lifestyle that were associated with having healthy diets. Smoking,^{8, 53–61} obesity,^{13–15} physical activity^{63, 64} and supplement use (reviewed^{28,29}), also associated with higher prevalence of nuclear cataract or cataract extraction in this and other studies, did not explain the associations with healthy diets in the present study. Yet, in practice, it is recognized that all aspects of healthy lifestyles are interrelated and improvement in each tends to increase the chances for improvement in other aspects.

There is a large body of observational studies that suggests that use of multivitamins is associated with lower risk for nuclear cataract (previously reviewed^{28, 29}). However, multivitamins were not associated with lower risk for cataract in the present study, even after considering longer-term use of multivitamins. The use of multivitamins is associated with diets that are higher in many nutrients and with other healthy behaviors.⁵⁴ The lack of association in the present sample of relatively healthy women could reduce the magnitude of confounding by healthy diet and lifestyle. Alternatively, multivitamins may only protect against nuclear cataract in people who already have poor diets. In the Linxian Cataract Study, conducted in a region of China with known high prevalence of micronutrient deficiencies, there was a 36% reduction in nuclear cataract among people 65–74 years old who used multivitamins.⁵⁵ Recently, multivitamin use for approximately nine years in a double-masked, placebo-controlled trial was observed to lower the development of nuclear opacities but raise risk for

posterior subcapsular opacities.⁵⁶ The lack of a protective association in the present study could result from the relatively healthy diets of women sampled.

The following additional limitations should be considered in drawing conclusions from the present study. Because the prevalence, rather than incidence, of nuclear cataract was assessed, the findings may theoretically represent poor diets which occur as a result of having nuclear cataracts or co-morbid conditions associated with them. However, this explanation for the protective association of diet and nuclear cataract is unlikely. Receiving diagnosis of chronic diseases are most likely to result in improved rather than worsened diet. Moreover, the associations of diet to nuclear cataract did not differ in older compared with younger women who would have been more likely to have chronic disease. Also, because the severity of nuclear sclerosis was assessed photographically, most women (52%) who had nuclear opacities of severity of four or greater had not been told by a doctor that they had a cataract. The HEI-95 scores in women who were told that they had a cataract (mean = 69) did not differ significantly ($p=0.16$) from those who were not told that they had a cataract (mean = 68). If anything, these data suggest that we may have underestimated, the magnitude of associations between healthy diets and the presence of nuclear cataract. Data from a few existing large, long-term prospective studies could potentially provide better estimates of the magnitude of these relationships and we hope these results will be forthcoming. Second, some risk factors were not measured, such as lead exposure⁵⁷, or may be unknown and may explain the associations observed. However, further adjusting for education, a marker of socioeconomic status which could reflect this or other unmeasured confounders did not alter ORs (not shown). Third, associations were limited to women in the present study and may not reflect the protective influence of diet in men. However, associations of single nutrients to nuclear cataract in men have been similar or stronger in other populations.^{20, 23} Finally, even though surgery for most cataracts in older white women can be presumed to result from cataracts in the nuclear region after age fifty⁶, some misclassification of nuclear cataract would have resulted from cataracts extracted due to opacities in the posterior subcapsular or cortical regions of the lens, possibly attenuating the associations between diet and nuclear cataracts. However, associations of diet index score with nuclear cataracts determined photographically in women with intact lenses in this sample were nearly identical (not shown.)

In conclusion, the present study adds to the body of literature that suggests that healthy diets are associated with lower risk for cataract. Diet was the strongest risk factor related to reduced risk for nuclear cataract in this sample of postmenopausal women. Smoking and obesity were also contributors. Lifestyle improvements that include healthy diets, smoking cessation and avoiding obesity may substantively lower the need for and economic burden of cataract surgery in aging American women.

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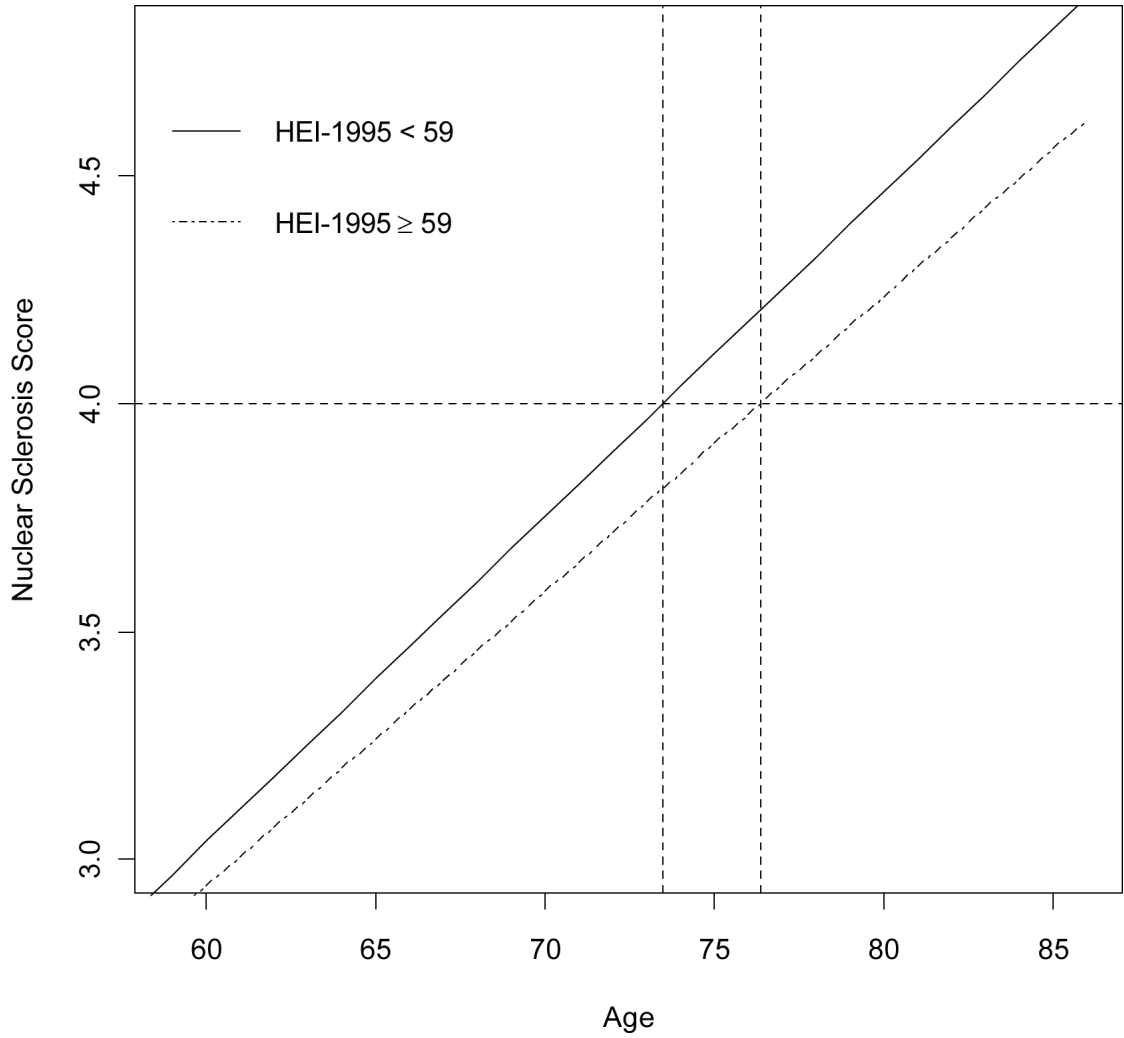


Figure. Nuclear sclerosis score by age at the time of photography for women with HEI-1995 score < 59 (quintile 1) vs. ≥ 59 (quintiles 2–5), in women with at least one intact lens (n=1,577). The vertical lines compare the ages at which nuclear sclerosis score is 4.0 (corresponding to clinically significant cataract) after adjusting for iris color, BMI, smoking (packyears) pulse pressure and physical activity (73.9 vs 76.3 years).

Table 1

Distribution of intake of food components which contribute to scores on the 1995 and 2005 Healthy Eating Indices (HEI) among women in CAREDS (n=1808).

	Percentile		Points
	10	90	
HEI-1995			
Components which contribute to high scores			
Servings/Day:			
Grain	1.5	4.6	10
Vegetables	1.6	6.9	10
Fruit	0.9	4.5	10
Milk or Dairy	0.7	3.1	10
Meat, Beans, Fish, or Eggs	0.9	2.8	10
Variety (different foods/mon)	41	67	10
Components which contribute to Lower Scores			
Total Fat (% of energy)	21	43	10
Saturated Fat (% of energy)	6.8	15.4	10
Cholesterol (mg/day)	84	343	10
Sodium (g/day)	1.5	4.4	10
HEI-2005			
Components which contribute to high scores			
Servings/Day:			
Grain			
Total	1.3	5.0	5
Whole	0.1	1.9	5
Vegetables			
Total	1.5	7.4	5
Dark Green, Orange, and Legume Vegetables	0.3	2.8	5
Fruit			
Total	0.8	4.4	5
Whole Fruit	0.5	3.6	5
Milk or Dairy	0.5	3.0	10
Meat, Beans, Fish, or Eggs	0.9	3.8	10
Oils (g/day)	2.8	25.1	10
Components which contribute to Lower Scores			
Saturated Fat (% of energy)	6.8	15.4	10
Sodium (g/day)	1.5	4.4	10

	Percentile		Points
	10	90	
Energy from Solid Fat, Alcohol, and Added Sugar (Kcal/day)	90	520	20

Table 2

Selected characteristics of women in CAREDS (n=1808) by high and low quintiles of 1995 Healthy Eating Index (HEI).

	Healthy Eating Index Quintile		P-value for trend
	Low 1	High 5	
HEI Range	28–58	81–94	
Demographic Risk Factors			
Age at CAREDS (median years) ^a	68	71	<0.001
Education (%>High School)	64	88	<0.001
Ethnicity (% Caucasian)	97	96	0.82
Nutritional Characteristics			
Fat (% total energy)	42	25	<0.001
Saturated fat (% total energy)	15	8	<0.001
Oils (g/d)	15	11	<0.001
Lutein and Zeaxanthin (median ug/d)	0.8	2.5	<0.001
Vitamin C (median mg/d)	54	157	<0.001
Vitamin E (median mg alpha tocopherols eq./d)	6.6	8.8	<0.001
Multivitamin Use (any,%)	39	52	<0.001
Multivitamin Use ^b (> 2 years, %)	39	56	<0.001
High Dose Antioxidants ^{b,c} (> 2 years)	19	31	0.005
Physical and Lifestyle Characteristics			
Age at CAREDS (median years) ^a			
Smoking Packyears (Mean for smokers)	20.0	11.7	<0.001
Past or current smoking (%)	44	37	0.13
Pulse Pressure (median mm Hg)	54.2	52.5	0.10
Body Mass Index (mm/kg ²)			<0.001
< 22.5	13	27	
22.5 ≤ to < 25	16	24	
25 ≤ to < 30	33	34	
30 ≤ to < 35	21	10	
35 ≤	17	5	

	Healthy Eating Index Quintile		P-value for trend
	Low 1	High 5	
History of Diabetes (%)	4.2	3.3	0.83
Family History of Cataract (%)	56	59	0.37
Average Annual Ocular UV-B Exposure Adult Lifetime (10^{-3} Maryland Sun Years)	5.6	6.2	0.58
Physical Activity (METS/day) (%)			<0.001
None – 3	40	11	
3 – 10	26	16	
10 – 21	20	35	
≥ 21	15	38	

^aValues are adjusted for age at CAREDS except for values of median age at CAREDS.

^bAssessed at CAREDS.

^cHigh dose antioxidants (at least 2 of 3): beta carotene $\geq 10,000$ IU, Vitamin C ≥ 120 , Vitamin E ≥ 60 .

Table 3

Adjusted odds ratios (95% confidence intervals) for nuclear cataract by age, healthy diet scores and other potential health, diet and risk factors^a among participants in the Carotenoids in Age-Related Eye Disease Study (N=1808)

Risk Factors	Nuclear Cataract or Extraction	
	Number with Outcome / At Risk 736/1808	
	Age adjusted	Multiple-variable adjusted ^b
Age at photography (per 10 years)	5.20 (4.35–6.26)	5.30 (4.36–6.48)
<i>P</i> -trend	<0.001	<0.001
Healthy Eating Index 1995 Score (Adjusted for Energy) (minimum, median, maximum)		
Quintile 1 (28,52,58), n=373	1.0	1.0
Quintile 2 (59,64,68), n=383	0.70 (0.50–0.96)	0.72 (0.52–1.00)
Quintile 3 (69,72,75), n=384	0.60 (0.43–0.84)	0.64 (0.45–0.90)
Quintile 4 (76,78,80), n=334	0.58 (0.41–0.82)	0.62 (0.43–0.89)
Quintile 5 (81,84,94), n=334	0.57 (0.40–0.81)	0.63 (0.43–0.91)
<i>P</i> -trend	0.001	0.01
Healthy Eating Index 2005 Score (minimum, median, maximum)		
Quintile 1 (44,62,65), n=362	1.0	1.0
Quintile 2 (65,67,69), n=362	0.86 (0.62–1.21)	0.91 (0.65–1.28)
Quintile 3 (69,71,72), n=361	0.79 (0.56–1.11)	0.81 (0.57–1.14)
Quintile 4 (72,74,76), n=362	0.68 (0.48–0.95)	0.71 (0.50–1.01)
Quintile 5 (76,78,87), n=361	1.03 (0.73–1.44)	1.12 (0.78–1.59)
<i>P</i> -trend	0.64	0.94
Healthy Eating Index 2005-Without Oil Subscore (minimum, median, maximum)		
Quintile 1 (41,56,60), n=362	1.0	1.0
Quintile 2 (60,62,64), n=362	0.79 (0.56–1.10)	0.81 (0.58–1.14)
Quintile 3 (64,66,67), n=361	0.75 (0.54–1.06)	0.80 (0.56–1.13)
Quintile 4 (67,69,70), n=362	0.70 (0.50–0.98)	0.74 (0.52–1.06)
Quintile 5 (70,72,80), n=361	0.66 (0.47–0.92)	0.72 (0.50–1.03)
<i>P</i> -trend	0.019	0.12
Alpha tocopherol from food (minimum, median, maximum mg/day)		
Quintile 1 (1,3,4), n=362	1.0	1.0
Quintile 2 (4,5,5), n=362	1.22 (0.87–1.70)	1.29 (0.92–1.81)
Quintile 3 (5,6,7), n=361	0.96 (0.69–1.35)	1.04 (0.74–1.48)
Quintile 4 (7,8,9), n=362	0.97 (0.70–1.36)	1.15 (0.80–1.65)
Quintile 5 (9,11,49), n=361	0.88 (0.63–1.24)	1.00 (0.70–1.43)
<i>P</i> -trend	0.19	0.52

	Nuclear Cataract or Extraction	
Risk Factors	Number with Outcome / At Risk 736/1808	
	Age adjusted	Multiple-variable adjusted ^b
Alpha tocopherol from food and supplements (minimum, median, maximum mg/day)		
Quintile 1 (3,13,19), n=362	1.0	1.0
Quintile 2 (19,26,39), n=362	1.05 (0.75–1.46)	1.08 (0.76–1.52)
Quintile 3 (39,46,54), n=361	0.94 (0.67–1.32)	1.02 (0.73–1.44)
Quintile 4 (56,215,425), n=362	0.83 (0.59–1.16)	1.08 (0.77–1.53)
Quintile 5 (426,450,8100), n=361	1.02 (0.73–1.42)	1.08 (0.77–1.53)
<i>P</i> -trend	0.63	0.50
Alpha tocopherol in serum (minimum, median, maximum umol/liter)		
Quintile 1 (0,28,32), n=357	1.0	1.0
Quintile 2 (32,35,39), n=357	0.74 (0.53–1.04)	0.81 (0.57–1.15)
Quintile 3 (39,43,48), n=357	0.93 (0.66–1.30)	1.06 (0.75–1.51)
Quintile 4 (48,55,62), n=357	0.70 (0.50–0.99)	0.81 (0.57–1.15)
Quintile 5 (62,76,200), n=356	0.98 (0.70–1.36)	1.08 (0.76–1.53)
<i>P</i> -trend	0.87	0.61
Vitamin C from food (minimum, median, maximum mg/day)		
Quintile 1 (9,40,57), n=362	1.0	1.0
Quintile 2 (57,72,92), n=362	1.00 (0.72–1.40)	1.14 (0.80–1.62)
Quintile 3 (92,109,128), n=361	0.80 (0.57–1.12)	0.94 (0.65–1.35)
Quintile 4 (128,149,173), n=362	0.70 (0.50–0.98)	0.87 (0.59–1.28)
Quintile 5 (173,207,503), n=361	0.70 (0.50–0.98)	0.86 (0.57–1.28)
<i>P</i> -trend	<0.001	0.05
Vitamin C from food and supplements (minimum, median, maximum mg/day)		
Quintile 1 (11,62,101), n=362	1.0	1.0
Quintile 2 (101,134,166), n=362	0.87 (0.62–1.21)	1.02 (0.72–1.45)
Quintile 3 (166,200,268), n=361	0.83 (0.59–1.16)	1.05 (0.73–1.50)
Quintile 4 (268,484,693), n=362	0.72 (0.51–1.00)	0.87 (0.61–1.24)
Quintile 5 (696,1120,20300), n=361	0.72 (0.51–1.00)	0.86 (0.60–1.22)
<i>P</i> -trend	0.063	0.094
Packyears:		
None, n=1051	1.0	1.0
0<x<7, n=407	1.13 (0.86–1.48)	1.17 (0.89–1.54)
≥ 7, n=350	1.61 (1.22–2.12)	1.53 (1.15–2.04)
<i>P</i> -trend	0.002	0.007
WHI Baseline BMI (mm/kg ²)		

	Nuclear Cataract or Extraction	
Risk Factors	Number with Outcome / At Risk 736/1808	
	Age adjusted	Multiple-variable adjusted ^b
22.5<x, n=350	1.27 (0.89–1.82)	1.29 (0.90–1.85)
22.5<=x<25, n=329	1.0	1.0
25<=x<30, n=658	1.37 (1.01–1.88)	1.34 (0.97–1.84)
30<=x<35, n=311	1.42 (0.99–2.04)	1.24 (0.86–1.80)
35<=x, n=160	2.01 (1.30–3.10)	1.61 (1.02–2.53)
<i>P</i> -trend	0.01	0.24
Pulse Pressure (sd=14.40 mmHg)	1.14 (1.02–1.27)	1.11 (1.05–1.39)
<i>P</i> -trend	0.03	0.09
Refractive Error (Diopters)		
–0.5 <	1.0	1.0
–2 < to ≤ –0.5	2.20 (1.68–2.88)	2.16 (1.64–2.84)
< –2	1.66 (1.28–2.17)	1.67 (1.28–2.20)
<i>P</i> -value	0.001	0.001
Iris pigmentation:		
Blue, n=752	1.0	1.0
Green, n=469	1.12 (0.86–1.46)	1.17 (0.89–1.54)
Light Brown, n=450	1.28 (0.98–1.68)	1.29 (0.98–1.70)
Dark Brown, n=1 37	1.84 (1.20–2.82)	1.82 (1.18–2.82)
<i>P</i> -value	0.004	0.004
Family History of Cataract, n=1013	1.07 (0.86–1.32)	1.10 (0.88–1.37)
<i>P</i> -value	0.55	0.41
Average Annual UVB Sunlight Exposure over Adult Lifetime (10 ^{–3} Maryland Sun Years) Per SD=0.0059	0.92 (0.83–1.03)	0.92 (0.82–1.02)
<i>P</i> -trend	0.16	0.12
Physical Activity (METS/day)		
< 3, n=408	1.0	1.0
3 ≤ x < 10, n=400	0.77 (0.56–1.06)	0.84 (0.61–1.16)
10 ≤ x < 21, n=495	0.75 (0.56–1.01)	0.87 (0.63–1.20)
≥ 21, n=493	0.73 (0.54–0.99)	0.89 (0.64–1.23)
<i>P</i> -value	0.054	0.46

^a All variables were assessed At WHI baseline except: history of asthma (determined at 3-year follow-up and family history of cataract and history of vitamin supplement use determined at CAREDS exam when photographs were taken.

^bThe multivariate model included: age, iris pigmentation (4 colors), 1995 Healthy Eating Index (except when the HEI-2005 was included in the model), Body Mass Index (5 categories), smoking (packyears), and pulse pressure and, for dietary variables, energy.

^cHigh dose antioxidants were defined as at least 2 of the following: beta carotene $\geq 10,000$ IU, Vitamin C ≥ 120 , Vitamin E ≥ 60 ; reference group = ≤ 2 years.