A prospective study of carotenoid intake and risk of cataract extraction in US men[1–3]

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ABSTRACT

Background: Dietary antioxidants, including carotenoids, are hypothesized to decrease the risk of age-related cataracts by preventing oxidation of proteins or lipids within the lens. However, prospective epidemiologic data concerning this phenomenon are limited.

Objective: Our objective was to examine prospectively the association between carotenoid and vitamin A intakes and cataract extraction in men.

Design: US male health professionals (n = 36 644) who were 45–75 y of age in 1986 were included in this prospective cohort study. Others were subsequently included as they became 45 y of age. A detailed dietary questionnaire was used to assess intake of carotenoids and other nutrients. During 8 y of follow-up, 840 cases of senile cataract extraction were documented.

Results: We observed a modestly lower risk of cataract extraction in men with higher intakes of lutein and zeaxanthin but not of other carotenoids (α-carotene, β-carotene, lycopene, and β-cryptoxanthin) or vitamin A after other potential risk factors, including age and smoking, were controlled for. Men in the highest fifth of lutein and zeaxanthin intake had a 19% lower risk of cataract relative to men in the lowest fifth (relative risk: 0.81; 95% CI: 0.65, 1.01; P for trend = 0.03). Among specific foods high in carotenoids, broccoli and spinach were most consistently associated with a lower risk of cataract.

Conclusions: Lutein and zeaxanthin may decrease the risk of cataracts severe enough to require extraction, although this relation appears modest in magnitude. The present findings add support for recommendations to consume vegetables and fruit high in carotenoids daily. *Am J Clin Nutr* 1999;70:517–24.

KEY WORDS Cataract, cataract extraction, diet, men, prospective studies, vitamin A, carotene, lutein, zeaxanthin, carotenoids, food-frequency questionnaire, Health Professionals Follow-up Study

INTRODUCTION

Cataract is an opacification of the lens that causes decreased visual acuity and can lead to blindness (1). Cataracts become more common with increasing age and are an important cause of disability among older adults; >1 million extractions are performed annually in the United States (2). Thus, identification of factors that could delay or prevent cataract development would be important both for increasing the well-being of older adults and for reducing medical care costs. Oxidative damage plays a major role in cataractogenesis and the intake of dietary antioxidants is hypothesized to help prevent cataract formation by blocking the oxidative modification of lens protein (3) or by preventing lipid peroxidation within the epithelium of the lens (4).

Much evidence suggests that elevated intakes or plasma concentrations of antioxidants are associated with decreased risk of cataract (5–16). However, the association between specific antioxidants and the risk of cataract is unclear. Also, in some studies, nutrient intakes of antioxidants were not associated with risk of cataract (16, 17). Frequent intake of fruit and vegetables has been associated with decreased risk of cataract in some, but not all, studies (6, 7, 14, 15). In an 8-y prospective study in women, Hankinson et al (6) reported that dietary carotene and total vitamin A intake were inversely associated with risk of cataract. Among specific foods, high intake of spinach, which is rich in lutein, was most consistently associated with a lower risk of cataract, whereas carrot intake (a major source of α-and β-carotene) showed no consistent relation with cataract.

Carotenoids can be effective antioxidants, especially at low partial pressures of oxygen such as in the lens (18, 19). Lutein and zeaxanthin may be particularly effective in protecting the eye because they are the only carotenoids accumulated by the retina and other ocular tissues (20–22). The extent to which blood

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carotenoid concentrations change with dietary manipulation varies between individuals (23). However, dietary supplementation with lutein and zeaxanthin increases the amount of macular pigment, which consists mainly of lutein and zeaxanthin (22). Macular lutein and zeaxanthin concentrations are inversely associated with lens density and may be markers for lutein and zeaxanthin in the lens (24). To evaluate these relations further in men, we examined prospectively the associations between dietary intake of vitamin A and specific carotenoids and the incidence of cataract extraction in participants enrolled in the Health Professionals Follow-up Study.

SUBJECTS AND METHODS

The Health Professionals Follow-up Study is a prospective investigation of dietary etiologies of chronic disease in 51 529 US male dentists, optometrists, osteopaths, podiatrists, pharmacists, and veterinarians who were aged 40–75 y in 1986. The men responded to a mailed questionnaire sent in February 1986 that elicited information on age, marital status, height and weight, ancestry, medication use, disease history, physical activity, and diet (described below). The men are followed up with mailed questionnaires every 2 y. The study protocol was approved by the Harvard School of Public Health.

Dietary assessment

To assess dietary intake, we used a semiquantitative food-frequency questionnaire. A description of the questionnaire and of the procedures for calculation of nutrient intakes were published previously (25). The questionnaire included 131 food items plus questions on vitamin and mineral supplements. The participants were asked about the average frequency of consumption of a given unit or portion size for each food during the previous year (eg, 1 apple or 1 slice of bread). There were 9 possible responses ranging from "never" to "≥6 times/d." Intake scores were calculated by summing the nutrient contribution of each food multiplied by its frequency of use, using food-composition data from the US Department of Agriculture (USDA), food manufacturers, and other published sources (26–28). The carotenoid food composition database contains values for the most commonly occurring carotenoids in fruit and vegetables, including α-carotene, β-carotene, lutein and zeaxanthin, β-cryptoxanthin, and lycopene. The carotenoid content of tomato-based food products was updated with values from the USDA (28). Although "lutein" intake represents both lutein and zeaxanthin intake, the main contributors to lutein intake (green leafy vegetables) contain essentially no zeaxanthin, and therefore lutein + zeaxanthin values for these foods represent primarily lutein (27). Peaches and corn contain both lutein and zeaxanthin in varying ratios (29). In addition to specific carotenoids, total vitamin A intake was assessed as preformed vitamin A (retinol from animal sources, supplements, and fortified foods) plus provitamin A carotenoids (provitamin A, primarily from fruit and vegetables). The derived values for provitamin A carotenoids accounted for most of the β-carotene intake, about half of the α-carotene intake, and a small fraction of the intake of other carotenoids. Energy-adjusted nutrients were calculated as the residuals after regression of each specific nutrient on total energy intake by using linear regression (30).

Data on the reproducibility and validity of the food-frequency questionnaire were published elsewhere (25). Correlation coefficients (adjusted for energy intake) between intake of antioxidant vitamins as assessed by the 1986 questionnaire and 2 wk of dietary records provided by a subsample of 127 men were 0.64 for carotene and 0.48 for total vitamin A (25). Among nonsmokers, intakes of specific dietary carotenoids were significantly correlated with the corresponding plasma concentrations for β-carotene (r = 0.30), α-carotene (r = 0.37), and lutein (r = 0.19), but not for lycopene (r = 0.01) (31).

In addition to recent diet, we also examined the relation between diet during high school and cataract risk. Questions about intake of foods during high school (age ≈13–18 y), including those high in carotenoids, were asked on the 1988 follow-up questionnaire. The abbreviated list of food items included apples, oranges or orange juice, broccoli or cauliflower, carrots, and spinach.

Other covariates

We included as covariates other known or suspected risk factors for cataract extraction that could distort associations with carotenoid and vitamin A intakes. Age, cigarette smoking, and diabetes are established risk factors for cataract (32–35). From the baseline questionnaire, we obtained information on age, body weight, height, diagnosis of diabetes, and past and present smoking habits. The number of cigarette pack-years of smoking was calculated by multiplying the number of packs (20 cigarettes) smoked per day by the number of years over which that amount was smoked. We chose pack-years as a measure of smoking status because cataract extraction has been more strongly related to cumulative dose of cigarette smoking than to recent exposure (32). Aspirin use, which was ascertained at baseline, has been hypothesized to decrease the risk of cataract (36). Alcohol consumption has been implicated in the pathogenesis of cataract in some studies (37, 38) and was assessed at baseline. Recreational physical activity influences insulin resistance and hyperglycemia and was assessed by using metabolic equivalents (METs), which represent multiples of the metabolic equivalent of sitting quietly for 1 h (39). We included area of residence to account for possible geographic variation in sun exposure, diet, and cataract extraction practices. To evaluate the influence of access to health care on cataract extraction, participants were asked how often they had visited an eye doctor in the previous 2 y.

Study population

We excluded from the analysis 2107 men who did not adequately complete the food-frequency questionnaire [≥70 items blank of 131 listed food items or reported intakes >17 600 kJ (4200 kcal) or <3350 kJ (800 kcal)/d]. In addition, we excluded men who reported on the 1986 questionnaire a diagnosis of cancer (except nonmelanoma skin cancer; n = 1960). These men might have recently altered their dietary pattern after diagnosis and, thus, the reported baseline diet might not have reflected long-term dietary intake. Men <45 y of age (n = 10 224) at baseline were excluded because they were not considered eligible to have senile cataracts; follow-up for these men began as they became 45 y of age. These exclusions (total of 14 885 men, including 594 baseline case exclusions as described below) left 36 644 men eligible for inclusion in the baseline population.

Case definition

Follow-up questionnaires were sent in 1988, 1990, 1992, and 1994 to all study participants to determine whether they had a variety of conditions including cataract extraction and, if so, we asked for permission to review their medical records. Dates of extraction were confirmed by medical record review. Other information abstracted from the medical records included date of initial diagnosis, any known cause of cataract, the participant's best-corrected visual acuity in each eye before surgery, and the location of the lens opacity (nuclear, cortical, posterior subcapsular, or any combination of the 3) in each eye. A total of 1969 men reported a first cataract extraction after the return of the 1986 questionnaires. Of these men, 274 (14%) either subsequently denied the diagnosis or had undergone cataract extraction before 1986; 1530 (78%) gave us permission to contact their ophthalmologist. Most of the ophthalmologists responded to our request (1415; 92%) and all confirmed the extractions. Because the confirmation rate was 100% and because all of the confirmed dates of extraction were within 6 mo of the participants' reports, we included 280 (14%) cases confirmed by the participants but for whom we had no information from their ophthalmologists, for a total of 1695 cases.

We excluded cataracts considered by the physicians to be either congenital or secondary to chronic steroid use, chronic intraocular inflammation, ocular trauma, previous intraocular surgery, or glaucoma (n = 66). Both the participant and his ophthalmologist indicated when the cataract had been extracted. We used the ophthalmologists' reported dates of extraction, and, if missing, the participants' reported extraction dates. Because we began follow-up in 1986, we excluded cases diagnosed before the 1986 questionnaire (n = 391), those with an unknown date of diagnosis (n = 131), and reported cases of extraction after January 1994, the end of the follow-up period (n = 6). After further exclusion of 261 cases with any of the factors described in the section above (eg, previous diagnosis of cancer), 840 cases remained for analysis.

Opacities may form in different areas of the lens (posterior subcapsular, cortical, or nuclear) and these types may have different etiologies (12, 14, 17). We therefore performed an additional analysis using each subtype as the outcome variable and examining the association with carotenoid intake. Three different case groups were defined on the basis of cataract subtype: nuclear, posterior subcapsular, and cortical only cataract in either eye if unilateral, or both eyes if bilateral, as determined by the participant's ophthalmologist. Those with more than one type of cataract were omitted from these subgroup analyses to minimize misclassification of opacity type.

Data analysis

Each participant's follow-up time began with the date of return of the 1986 questionnaire or the date they turned 45 y of age, whichever occurred first. Follow-up continued until the report of cataract, death, cancer, or February 1, 1994, for a total of 307 259 person-years of follow-up.

In our primary analysis, age was updated at the beginning of each 2-y interval because we included individuals as they became 45 y old. Baseline values for nutrients and other exposures were carried forward throughout the follow-up period because cataracts develop over many years. To reduce the effect of measurement error associated with a single questionnaire (40), we also conducted analyses using the cumulative average of carotenoid intakes. In this analysis, we used the carotenoid intake from the 1986 questionnaires for the 1986–1990 follow-up and the average intakes from both the 1986 and 1990 dietary questionnaires for the 1990–1994 follow-up. Other covariates (including body mass index, age, alcohol intake, and smoking) were updated at the start of each 2-y interval. For exposures that were not updated in this analysis (number of physician visits, physical activity, and area of residence), the initial value was carried forward throughout the follow-up period. The SAS computer analysis program (version 6; SAS Institute, Cary, NC) was used for the statistical analyses.

Relative risks (RRs) were first calculated by dividing the incidence rate of cataract extraction in men in each category of nutrient intake by the rate for the men in the lowest category. RRs adjusted for age (in 5-y categories) were derived by the Mantel-Haenszel method (41). The Mantel extension test was used to test for linear trends (42). To adjust for other risk factors, we used pooled logistic regression with 2-y time intervals to estimate rate ratios (43). In multivariate logistic models, we tested for significant monotonic trends by assigning each participant the median value for the category and modeling this value as a continuous variable. We assessed possible interactions between nutrient intake, smoking status, and diabetes using the likelihood ratio test. All P values were two sided.

RESULTS

Nutrient intake

Intakes of provitamin A carotenoids and lutein and zeaxanthin were associated with a moderately decreased risk of cataract extraction in analyses adjusted for age (**Table 1**). When these relations were examined after several additional potential risk factors were controlled for—including cigarette smoking, body mass index, history of diabetes, energy and alcohol intake, area of residence in 1986, aspirin use, whether participants had undergone an eye exam between 1988 and 1990, and time period—the RRs were all attenuated. In the multivariate analyses, the trend of decreased risk of first cataract extraction with increasing intake of antioxidants remained significant only for lutein and zeaxanthin. Men in the highest fifth of lutein and zeaxanthin intake had a 19% lower risk of cataract relative to men in the lowest fifth (RR: 0.81; 95% CI: 0.65, 1.01; P for trend = 0.03). This inverse association was not materially altered when we included terms for duration of vitamin supplement use (vitamins C or E, or multivitamins) in the multivariate model. We found similar results for the cumulatively updated nutrients. For example, the multivariate RR when comparing the lowest and highest quintiles of intake for lutein and zeaxanthin was 0.78 (95% CI: 0.62, 0.98; P for trend = 0.01). We also found similar results when we examined a wider range of intake by comparing the top decile (median: 8745 μg/d) with the lowest quintile (median: 1300 μg/d) of intake. Men in the top decile had a significantly lower risk than did those in the lowest quintile of intake (RR: 0.78; 95% CI: 0.59, 1.03; P for trend = 0.02).

We examined the influence of smoking and diabetes on the association between carotenoid intake and cataract risk. The inverse association between lutein and zeaxanthin intake and cataract appeared strongest among never smokers (**Table 2**), but a formal test of interaction with smoking was not significant. The relations with other carotenoids were essentially null in smokers and nonsmokers. The differences in RR by diabetes status were not significant; however, we had limited power to detect interactions because there were so few cases in diabetics. Exclusion of diabetics from the total group did not appreciably alter the RRs for other carotenoids.

Next, we evaluated the association with nutrient intakes separately for cataract subtypes. There were 207 nuclear, 136 posterior subcapsular, and 46 cortical cataracts. The remaining

TABLE 1
Relative risk (RR) of cataract extraction in men from 1986 to 1994 for energy-adjusted carotenoid intake as assessed in 1986[1]

Nutrient	Quintile of intake 1	2	3	4	5	*P* for trend
Carotene with supplements (IU)						
Median intake	3777	5770	7782	11 231	18 499	
Cases (*n*)	142	164	181	178	175	
Age-adjusted RR	1.00	1.02	1.05	0.96	0.87	0.03
Multivariate RR	1.00	1.02	1.05	0.94	0.85	0.05
95% CI		0.81, 1.28	0.84, 1.31	0.75, 1.18	0.68, 1.07	
α-Carotene (μg)						
Median intake	292	473	634	1010	1886	
Cases (*n*)	156	164	162	181	177	
Age-adjusted RR	1.00	1.05	0.95	1.02	0.88	0.13
Multivariate RR	1.00	1.07	0.96	1.04	0.89	0.18
95% CI		0.86, 1.34	0.77, 1.20	0.84, 1.30	0.72, 1.11	
β-Carotene (μg)						
Median intake	2046	3136	4225	5806	9214	
Cases (*n*)	136	169	174	181	180	
Age-adjusted RR	1.00	1.11	1.06	1.01	0.93	0.11
Multivariate RR	1.00	1.13	1.07	0.99	0.92	0.14
95% CI		0.90, 1.42	0.85, 1.34	0.79, 1.24	0.73, 1.16	
Lycopene (μg)						
Median intake	3413	6159	8692	12 212	18 901	
Cases (*n*)	164	159	171	163	183	
Age-adjusted RR	1.00	1.05	1.10	1.02	1.10	0.49
Multivariate RR	1.00	1.05	1.11	1.01	1.10	0.54
95% CI		0.84, 1.31	0.89, 1.38	0.81, 1.26	0.88, 1.36	
β-Cryptoxanthin (μg)						
Median intake	10.8	33.2	56.2	92.5	175.1	
Cases (*n*)	142	157	161	193	187	
Age-adjusted RR	1.00	1.14	1.07	1.21	1.04	0.97
Multivariate RR	1.00	1.20	1.12	1.28	1.09	0.76
95% CI		0.95, 1.50	0.89, 1.41	1.03, 1.60	0.87, 1.37	
Lutein and zeaxanthin (μg)						
Median intake	1300	2279	3182	4342	6871	
Cases (*n*)	173	180	181	153	153	
Age-adjusted RR	1.00	1.01	0.97	0.82	0.80	0.01
Multivariate RR	1.00	1.00	0.98	0.83	0.81	0.03
95% CI		0.81, 1.23	0.79, 1.20	0.67, 1.04	0.65, 1.01	
Retinol (IU)						
With supplements						
Median intake	1056	1933	3078	6218	12 598	
Cases (*n*)	148	148	194	160	190	
Age-adjusted RR	1.0	0.93	1.10	0.89	0.99	0.70
Multivariate RR	1.0	0.92	1.08	0.87	0.96	0.56
95% CI		0.73, 1.16	0.87, 1.34	0.69, 1.09	0.77, 1.19	
No supplements (IU)						
Median intake	873	1440	2028	2788	5079	
Cases (*n*)	132	161	171	198	178	
Age-adjusted RR	1.0	1.17	1.18	1.22	1.06	0.94
Multivariate RR	1.0	1.17	1.17	1.20	1.04	0.72
95% CI		0.93, 1.47	0.93, 1.47	0.96, 1.50	0.83, 1.31	
Vitamin A (IU)						
With supplements						
Median intake	6252	9249	12 713	17 335	27 222	
Cases (*n*)	145	155	172	184	184	
Age-adjusted RR	1.0	0.86	0.89	0.88	0.82	0.09
Multivariate RR	1.0	0.87	0.87	0.86	0.80	0.10
95% CI		0.69, 1.09	0.70, 1.09	0.70, 1.07	0.64, 1.00	
No supplements (IU)						
Median intake	5683	8047	10 388	13 890	20 694	
Cases (*n*)	144	157	183	175	181	
Age-adjusted RR	1.0	0.91	0.98	0.89	0.83	0.10
Multivariate RR	1.0	0.91	0.97	0.88	0.81	0.06
95% CI		0.73, 1.14	0.78, 1.21	0.70, 1.10	0.64, 1.01	

[1] Each logistic model included terms for age (5-y categories), time period (2-y intervals), diagnosis of diabetes (yes or no), cigarette smoking (never or 1–44 or >44 pack-years), BMI (quintile), area of US residence (east, central, west, or Texas, California, or Florida), aspirin use (yes or no), energy intake (quintile), physical activity (quintile of metabolic equivalents), alcohol intake (0, 1–4, 5–9, 10–14, 15–29, ≥30 g/d), routine eye exams (yes or no), and profession.

TABLE 2
Multivariate-adjusted relative risk and 95% CI of cataract extraction by lutein and zeaxanthin intake within smoking category[1]

	Quintile of intake					
Smoking (pack-years)[2]	1	2	3	4	5	*P* for trend
Never (*n* = 294)	1.00	1.02 (0.73, 1.46)	0.96 (0.67, 1.36)	0.71 (0.49, 1.04)	0.71 (0.49, 1.03)	0.02
1–44 (*n* = 359)	1.00	1.06 (0.76, 1.48)	0.94 (0.67, 1.33)	0.99 (0.73, 1.39)	0.87 (0.62, 1.23)	0.32
≥45 (*n* = 144)	1.00	0.97 (0.59, 1.60)	1.14 (0.70, 1.88)	0.77 (0.44, 1.35)	1.00 (0.59, 1.70)	0.83

[1] Each logistic model included terms for age (5-y categories), time period (2-y intervals), diagnosis of diabetes (yes or no), BMI (quintile), area of US residence (east, central, west, or Texas, California, or Florida), aspirin use (yes or no), energy intake (quintile), physical activity (quintile of metabolic equivalents), alcohol intake (0, 1–4, 5–9, 10–14, 15–29, ≥30 g/d), routine eye exams (yes or no), and profession.

[2] Values add to less than total number of cases because of missing information.

451 cataracts were classified as having either a combination of the 3 types or were missing this information. Because of sparse data for cortical cataracts, we limited our analyses to nuclear and posterior subcapsular cataract types. In multivariate models, those in the highest quintile of intake of lycopene had a reduced risk of nuclear cataract (RR: 0.69; 95% CI: 0.44, 1.10; *P* for trend = 0.05) but not of posterior subcapsular cataract (RR: 1.36; 95% CI: 0.82, 2.25; *P* for trend = 0.13). No other substantial differences were noted between subtypes, and the relations given above were similar to those reported for all extractions combined.

Food intake

On the basis of our findings of an inverse association between lutein and zeaxanthin intake and cataract extraction, we assessed the associations with intakes of individual foods high in carotenoids (**Table 3**). When added to the basic multivariate model one at a time, increasing frequency of intakes of broccoli and cooked spinach were each associated with a significantly decreased risk of cataract extraction. Consumption of broccoli and spinach each showed a consistent inverse relation with cataract after these and other foods rich in carotenoids were added simultaneously into the multivariate model. Kale, a vegetable rich in lutein, was not associated with cataract extraction, although few men reported intakes ≥1 time/wk. There was no association between intake of other leafy green vegetables (iceberg lettuce and romaine lettuce) and cataract extraction. Intake of corn, a primary source of zeaxanthin, also appeared unrelated to risk of cataract extraction. No other associations with specific fruit or vegetables were observed.

Because cataract develops over many years, we hypothesized that frequent consumption of foods high in carotenoids early in life or for long periods of time may be associated with a lower risk of senile cataract extractions. We therefore examined the risk of cataract extraction according to food intake during high school and for those with consistent long-term intake of vegetables (including those rich in carotenoids). Among foods high in carotenoids that were included in the questionnaire about intake during high school, intakes of broccoli, spinach, and carrots were not significantly associated with decreased risk. We further examined the risk of cataract in the subjects classified jointly according to their intake in high school and intake reported in 1986. When subjects were classified jointly according to frequency of intake of specific foods, men consuming broccoli >2 times/wk both early in life and in 1986 had the lowest risk of senile cataract compared with those in the opposite extreme, although the association was not significant (RR: 0.77; 95% CI: 0.49, 1.21). The comparable RR for intake of spinach both early in life and in 1986 was similar (RR: 0.71; 95% CI: 0.46, 1.10). Joint classification of intake of carrots did not reveal an association with cataract risk.

When we examined the risk of cataract in participants who did not change their intake of vegetables in the 10 y before completing the dietary questionnaire (511 cases; 169 399 person-years), the multivariate RR for the comparison of the lowest with the highest quintile of lutein and zeaxanthin intake was 0.80 (95% CI: 0.60, 1.07; *P* for trend = 0.06). There were no other significant associations between cataract extraction and other carotenoids (α-carotene, β-carotene, lycopene, and β-cryptoxanthin). Intakes of spinach and broccoli were also each associated with a significantly decreased risk of cataract extraction among participants who did not change their intake of vegetables for 10 y.

DISCUSSION

In this large prospective study, we observed a modest inverse association between intake of lutein and zeaxanthin and extraction of cataracts. Men in the highest fifth of lutein and zeaxanthin intake had a 19% lower risk of cataract extraction compared with those in the lowest fifth of intake. There was no significant association between intake of vitamin A or other carotenoids and risk of cataract in multivariate analyses. Increased consumption of some foods high in lutein, including broccoli and spinach, was associated with a lower risk of cataract extraction. The finding that increased intake of other fruit and vegetables was not associated with a decreased risk suggests that the relation may be specifically due to lutein and zeaxanthin and not simply to a healthy lifestyle.

Our finding of an apparently protective effect of lutein and zeaxanthin and lutein-rich foods on risk of cataract extraction agrees with other studies investigating the relation between dietary carotenoids and risk of cataract. In the largest study, Hankinson et al (6) observed in the Nurses' Health Study that among specific food items, spinach was most consistently associated with a lower risk. Mares-Perlman et al (13) found a higher concentration of carotenoids, including serum lutein, to be significantly related to a lower risk for nuclear sclerosis. Our findings are also consistent with those of other studies reporting a lower risk of cataract in people with high serum concentrations of carotenoids or high intakes of foods rich in carotenoids (7, 8, 12, 15).

Vitamin A intake was associated with a modest but nonsignificantly decreased risk of cataract extraction in this cohort of men. In an earlier report of a study in women, vitamin A was associated with a 39% decreased risk of cataract extraction (6). Updated analyses, which included a larger number of cases, showed a more modest RR of 0.87 (95% CI: 0.66, 1.15; *P* for

TABLE 3
Relative risk (RR) of cataract extraction from 1986 to 1994 by frequency of consumption of foods rich in carotenoids as assessed in 1986[1]

Food[2]	Frequency				P for trend
	<1 time/mo	1–3 times/mo	1 time/wk	>2 times/wk	
Broccoli					
Cases (n)	133	275	256	160	
Age-adjusted RR	1.00	0.86	0.79	0.71	0.003
Multivariate RR	1.00	0.89	0.83	0.77	0.02
95% CI		0.73, 1.09	0.67, 1.02	0.61, 0.97	
Carrots					
Cases (n)	76	288	216	247	
Age-adjusted RR	1.00	1.01	0.82	0.87	0.04
Multivariate RR	1.00	1.02	0.83	0.88	0.06
95% CI		0.80, 1.30	0.65, 1.07	0.68, 1.12	
Raw spinach					
Cases (n)	494	222	65	19	
Age-adjusted RR	1.00	0.88	0.88	0.70	0.03
Multivariate RR	1.00	0.90	0.89	0.73	0.04
95% CI		0.77, 1.05	0.68, 1.15	0.46, 1.16	
Cooked spinach					
Cases (n)	360	320	114	18	
Age-adjusted RR	1.00	1.02	0.97	0.52	0.09
Multivariate RR	1.00	1.02	0.97	0.51	0.08
95% CI		0.88, 1.19	0.78, 1.20	0.32, 0.82	
Kale					
Cases (n)	673	79	23	11	
Age-adjusted RR	1.00	1.03	0.93	0.83	0.66
Multivariate RR	1.00	1.06	0.98	0.85	0.86
95% CI		0.84, 1.34	0.65, 1.49	0.47, 1.56	
Corn					
Cases (n)	129	339	233	118	
Age-adjusted RR	1.00	0.96	0.90	0.95	0.46
Multivariate RR	1.00	0.97	0.92	0.99	0.72
95% CI		0.80, 1.17	0.74, 1.14	0.77, 1.27	
Yellow squash					
Cases (n)	411	281	95	27	
Age-adjusted RR	1.00	0.96	0.85	0.70	0.04
Multivariate RR	1.00	0.99	0.87	0.72	0.05
95% CI		0.85, 1.15	0.70, 1.09	0.49, 1.05	
Sweet potatoes					
Cases (n)	417	305	81	22	
Age-adjusted RR	1.00	1.02	1.03	0.73	0.54
Multivariate RR	1.00	1.05	1.08	0.76	0.74
95% CI		0.90, 1.22	0.84, 1.38	0.49, 1.18	
Tomatoes					
Cases (n)	39	103	178	507	
Age-adjusted RR	1.00	0.85	0.90	0.93	0.78
Multivariate RR	1.00	0.87	0.89	0.91	0.97
95% CI		0.62, 1.22	0.65, 1.22	0.68, 1.21	
Tomato sauce					
Cases (n)	197	364	173	78	
Age-adjusted RR	1.00	1.02	0.82	0.81	0.01
Multivariate RR	1.00	1.09	0.87	0.89	0.07
95% CI		0.92, 1.29	0.71, 1.06	0.68, 1.16	
Cantaloupe					
Cases (n)	246	307	164	84	
Age-adjusted RR	1.00	0.83	0.88	0.88	0.24
Multivariate RR	1.00	0.86	0.90	0.87	0.11
95% CI		0.73, 1.01	0.74, 1.09	0.68, 1.11	

[1] Each logistic model included terms for age (5-y categories), time period (2-y intervals), diagnosis of diabetes (yes or no), cigarette smoking (never or 1–44 or >44 pack-years), BMI (quintile), area of US residence (east, central, west, or Texas, California, or Florida), aspirin use (yes or no), energy intake (quintile), physical activity (quintile of metabolic equivalents), alcohol intake (0, 1–4, 5–9, 10–14, 15–29, ≥30 g/d), routine eye exams (yes or no), and profession.
[2] Values add to less than total number of cases because of missing responses for specific foods.

trend = 0.04) (44). Our RR estimate was similar and the lack of statistical significance may have been due to the smaller number of cases (*n* = 840 for men compared with 1471 for women).

Assessment of nutritional antioxidant status at the time of cataract diagnosis may not be valid unless it can be assumed that current nutritional status reflects past nutritional status. The assessment of diet in this study was made before diagnosis. We were also able to examine the possible relation between intake of foods rich in carotenoids earlier in life and risk of cataract. Recall of diet from high school is reasonably reproducible and may be sufficiently precise to assess the influence of remote diet in epidemiologic studies (45). Spearman correlations between reported vegetable intake in high school and that reported in 1986 ranged between 0.20 and 0.41. We did not find a significant association between intake of broccoli and spinach early in life and decreased risk of cataract. However, when subjects were classified jointly according to their dietary pattern in high school and that reported in 1986, those consuming broccoli and spinach most frequently both early in life and in 1986 tended to have the lowest risk of cataract extraction.

Cigarette smoking is associated with increased lipid peroxidation (46), low plasma antioxidant concentrations (47), and an increased risk of cataract (6, 32–34). Thus, we hypothesized that the association between cataract and carotenoid intake might vary by smoking status. The protective effect of lutein and zeaxanthin appeared somewhat stronger in never smokers, as expected, but interaction terms added to the multivariate models were not significant. We had limited power to test this interaction because only 10% of men were current smokers in 1986. The potential interaction between smoking and risk of cataract requires further evaluation with additional follow-up in this and other cohorts.

Each cataract type has unique biochemical properties and thus may be initiated by different factors (12, 14, 17). We examined the risk of cataract extraction by cataract subtype and found that most associations were similar across types, although those within the highest quintile of lycopene intake had a reduced risk of nuclear cataract ($P = 0.05$). However, Mares-Perlman et al (13, 14) reported an odds ratio of 1.10 (95% CI: 0.71, 1.72) for severe nuclear sclerosis in the highest compared with the lowest quintile for usual daily intake of lycopene. Thus, given the discrepant results from other reports and the small number of cases (*n* = 208) of nuclear-only cataract in our cohort, these findings must be interpreted with caution. Because cataract subtype was not assessed in a standard manner and documentation in medical records may be imperfect, some cases were likely misclassified by specific type. Although these errors are unlikely to be associated with dietary intake, their effect would tend to bias RRs toward the average effect seen with all cases combined, thus making type-specific associations more difficult to detect.

We were unable to assess "incident" cataracts because repeated ophthalmologic examination of this large cohort in a standardized manner would be impossible. Therefore, the procedure of cataract extraction was used to define the occurrence of disease. By restricting the analysis to these cases, we were unlikely to include false-positive cases. Although there were men with cataracts not requiring extraction in our noncase group, underascertainment of cases, if not related to exposure status, would not bias the RR in a cohort study (41). The use of cataract extraction rather than cataract diagnosis as an endpoint decreases the chance for variation in the threshold for diagnosis of disease. Because all participants are health professionals, access to medical care is likely to be more uniform than in the general population. Our results could be biased if men who were more health conscious and likely to consume diets high in carotenoids also tended to have cataracts extracted at either an earlier or later stage. To examine this issue, we assessed the Spearman correlation between each nutrient and visual acuity before surgery in the eye being operated on as an index of disease severity. These correlations were all very small (range: from −0.17 to 0.11). Also, controlling for whether subjects had an eye exam between 1988 and 1990 did not alter the nutrient coefficients in the multivariate models. Men in the highest fifth of intake for each nutrient were just 2–6% more likely to be examined by a doctor in 1988–1990 than were those in the lowest fifth. Therefore, any bias from using cataract extraction as the endpoint is likely to be small and, if anything, it would understate the inverse relation with lutein and zeaxanthin intake.

Data on exposures were collected before diagnosis; thus, any misclassification would be unrelated to risk of cataract and would tend to bias our results toward the null. The high follow-up rate in this cohort (average: 94% biennially), minimizes this as a source of bias.

Our findings strengthen the evidence that dietary carotenoids, and specifically lutein and zeaxanthin, may lower the incidence of cataracts severe enough to require extraction. Although further study of carotenoid intake and cataract is warranted, including a more detailed evaluation by cataract subtype and important risk factors such as smoking, the present findings support recommendations to consume vegetables and fruit high in carotenoids daily (48).

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