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Nutrient intake and cataract extraction in women: a prospective study

Susan E Hankinson, Meir J Stampfer, Johanna M Seddon, Graham A Colditz, Bernard Rosner, Frank E Speizer, Walter C Willett

Abstract

Objective—To examine prospectively the association between dietary intake of vitamins C and E, carotene, and riboflavin and cataract extraction in women.

Design—Prospective cohort study beginning in 1980 with eight years of follow up.

Setting—11 states of the United States.

Participants—Female registered nurses who were 45 to 67 years of age. 50 828 women were included in 1980 and others were added as they became 45 years of age.

Main outcome measure—Incidence of extraction of senile cataracts.

Results—493 cataracts were extracted during 470 302 person years of follow up. Intake of carotene and vitamin A was inversely associated with cataract: in multivariate analyses, women in the highest fifth of total vitamin A intake (excluding supplements) had a 39% lower risk of cataract relative to women in the lowest fifth (relative risk 0·61; 95% confidence interval 0·45 to 0·81). Neither riboflavin nor dietary vitamins E or C were associated with cataract in a multivariate analysis. Among specific food items spinach (rather than carrots, the greatest source of β carotene) was most consistently associated with a lower relative risk. The risk of cataract was 45% lower among women who used vitamin C supplements for 10 or more years (relative risk 0·55 (0·32 to 0·96)), but no association was noted for multivitamin intake.

Conclusion—Dietary carotenoids, although not necessarily β carotene, and long term vitamin C supplementation may decrease the risk of cataracts severe enough to require extraction.

Introduction

Cataracts occur commonly with increasing age.[1] Cataract extraction surgery is generally successful but accounts for 12% of the Medicare budget in the United States.[2] Delaying the onset of cataracts by 10 years could reduce the need for surgery by 45%[3]; however, the means of modifying risk has not been established.

One likely mechanism of cataract formation is protein oxidation and precipitation.[4,5] Several vitamins may prevent cataract formation by preventing oxidation of the lens proteins. Vitamins C and E and β carotene are antioxidants, and riboflavin is part of flavin adenine dinucleotide, a cofactor for the antioxidant enzyme glutathione reductase.[6] Protective effects of vitamins C, E, and riboflavin have been suggested in animal studies[6-13] and in vitro experiments.[11,14,15]

Moderate to strong inverse associations between risk of cataracts and dietary intake or plasma concentrations of vitamin C,[16-19] vitamin E,[18-20] riboflavin,[19-21] and carotene[16] have been found in some epidemiological studies but not in others.[22-24] These studies have all been cross sectional or retrospective in design. In addition, several have been small[16,21] or have collected limited data on diet[18,23,24] or other cataract risk factors.[21] Therefore we prospectively examined the associations between intakes of vitamins C and E, riboflavin, carotene, and preformed vitamin A and the incidence of cataract extraction in a large cohort of American women during eight years of follow up.

Methods

The Nurses' Health Study began in 1976 among 121 700 female registered nurses 30-55 years of age and residing in one of 11 states[25]; they are followed by biennial postal questionnaires. In 1980, a previously described semiquantitative food frequency questionnaire was sent to participants,[26] asking about their usual frequency of consuming certain foods over the past year, with nine options ranging from once or less a month to more than six times a day. 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, food manufacturers, and other published sources.[27,28] Vitamin A intake was assessed as preformed vitamin A (retinol, from animal sources and vitamin fortified foods) and carotene (provitamin A, primarily from fruits and vegetables). The derived values for carotene[29] correspond to most of the β carotene intake, about half of the α carotene, and a small fraction of intake of other carotenoids. We assessed the validity of the study's questionnaire extensively.[26] Correlations (adjusted for energy intake) between intake of antioxidant vitamins as assessed by the questionnaire and four one week records of diet collected over one year ranged from 0·36 for total vitamin A without supplements to 0·75 for vitamin C with supplements.

Duration of use of multivitamins and specific vitamin A, C, and E supplements was asked in 1980 and has been updated every two years. We collected detailed information on intake of foods rich in carotenoids in 1982 and sent out a 116 item questionnaire in 1984. Smoking status, height, weight, and diagnosis of diabetes and hypertension were asked in 1976 and, except for height, have been updated biennially. In 1980, 1982, and 1986 use of aspirin was ascertained.

The 1980 questionnaire was completed by 98 462 cohort members. Women who left 10 or more items blank (4%), had implausible total food scores (2·7%), or reported a diagnosis of cancer (except non-melanoma skin cancer) were excluded from this analysis. Women under 45 years of age were excluded as they were not considered eligible to have senile cataract; these women were added to the analysis as they became 45 years of age. These exclusions left 50 828 women in the 1980 baseline population. Women

Channing Laboratory, Department of Medicine, Harvard Medical School and Brigham and Women's Hospital, Boston, MA 02115, USA
Susan E Hankinson, *research associate*
Graham A Colditz, *associate professor of medicine*
Bernard Rosner, *professor of medicine (biostatistics)*
Frank E Speizer, *professor of medicine*

Harvard School of Public Health, Boston, MA 02115
Meir J Stampfer, *associate professor of epidemiology*
Walter C Willett, *professor of nutrition*

Harvard Medical School and Massachusetts Eye and Ear Infirmary, Boston, MA 02115
Johanna M Seddon, *associate professor of ophthalmology*

Correspondence and requests for reprints to: Dr S E Hankinson, Channing Laboratory, 180 Longwood Avenue, Boston, MA 02115, USA.

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contributed time in each two year interval until the report of a cataract extraction, cancer, death, or until 1 June 1988, for a total of 470 302 person years.

In 1984, 1986, and 1988 participants were asked if they had had a cataract extraction. When a woman reported an extraction and granted permission to review medical records we contacted the ophthalmologist to confirm the dates of initial diagnosis and extraction and to determine any known cause of the cataract. A total of 805 participants reported a first cataract extraction after the return of their 1980 questionnaire. Seven hundred and sixty nine women (96%) permitted us to contact the ophthalmologist; 687 ophthalmologists responded and all confirmed the extraction. Because the confirmation rate was 100% and because 91% of the confirmed dates of extraction were within six months of the nurses' reports we included cases confirmed by the nurse but for whom we had no information from the ophthalmologist.

Women whose cataracts were extracted before age 45 or were considered by the physician to be either congenital or secondary to chronic steroid use, chronic intraocular inflammation, ocular trauma, or previous intraocular surgery were excluded (n=108). Both the participant and her ophthalmologist indicated when a cataract had first been diagnosed. The earlier of the two dates was used to exclude 156 women diagnosed before completion of the 1980 questionnaire because knowledge of cataract might have altered diet or other variables of interest. Twelve women were unable to recall the year of diagnosis or surgery and were excluded, leaving 493 cases for this analysis.

For each participant without a reported cataract extraction, follow up time equal to the number of months between the return of the 1980 questionnaire and return of the 1982 questionnaire was assigned to each covariate according to its status in 1980. Similarly, for each subsequent two year interval, additional months of follow up were assigned according to the updated exposures at the beginning of the interval.

Nutrients were adjusted for total energy intake and standardised to 1600 kcal (6·7 MJ)/day as described elsewhere[30] and categorised by quintiles. The adjusted nutrients represent the nutrient composition of the diet with total energy held constant, as would be done in an

TABLE I—*Relative risk of cataract extraction from 1980 to 1988 by fifth of energy adjusted nutrient intake as assessed in 1980. Values for nutrient intake are medians for the fifth*

	Fifth of intake					
Nutrient	1	2	3	4	5	p Value for trend
Carotene (IU)	2935	4707	6610	9456	14 558	
Adjusted for age*	1·0	1·09	0·80	0·68	0·70	<0·001
Multivariate model	1·0	1·09	0·80	0·66	0·73	<0·001
(95% confidence interval)†		(0·84 to 1·43)	(0·60 to 1·07)	(0·48 to 0·97)	(0·55 to 0·97)	
Retinol (IU):						
With supplements (IU)	853	1860	2706	5815	10 426	
Adjusted for age	1·0	0·79	0·80	0·84	0·91	0·70
Multivariate model	1·0	0·83	0·85	0·88	0·98	0·94
(95% confidence interval)‡		(0·62 to 1·12)	(0·64 to 1·14)	(0·66 to 1·17)	(0·74 to 1·30)	
No supplements	717	1569	2056	2705	5451	
Adjusted for age	1·0	0·86	0·68	0·68	0·73	0·01
Multivariate model	1·0	0·82	0·71	0·70	0·77	0·03
(95% confidence interval)‡		(0·62 to 1·09)	(0·53 to 0·95)	(0·52 to 0·93)	(0·59 to 1·02)	
Total vitamin A (IU)						
With supplements	5119	8029	11 101	14 806	22 467	
Adjusted for age	1·0	0·70	0·78	0·74	0·66	0·01
Multivariate model	1·0	0·70	0·79	0·77	0·68	0·02
(95% confidence interval)†		(0·52 to 0·94)	(0·60 to 1·05)	(0·59 to 1·02)	(0·51 to 0·90)	
No supplements	4715	6951	9301	12 376	17 924	
Adjusted for age	1·0	0·99	0·79	0·67	0·59	<0·001
Multivariate model	1·0	0·99	0·81	0·69	0·61	<0·001
(95% confidence interval)†		(0·75 to 1·30)	(0·61 to 1·08)	(0·52 to 0·92)	(0·45 to 0·81)	
Riboflavin (mg):						
With supplements	1·2	1·5	1·9	2·8	5·0	
Adjusted for age	1·0	0·86	0·82	0·87	0·88	0·43
Multivariate model	1·0	0·89	0·83	0·87	0·91	0·57
(95% confidence interval)‡		(0·67 to 1·18)	(0·62 to 1·11)	(0·65 to 1·15)	(0·69 to 1·20)	
No supplements	1·2	1·4	1·6	1·9	2·3	
Adjusted for age	1·0	0·86	0·84	0·78	0·74	0·03
Multivariate model	1·0	0·92	0·89	0·83	0·78	0·06
(95% confidence interval)‡		(0·70 to 1·21)	(0·67 to 1·18)	(0·63 to 1·10)	(0·59 to 1·03)	
Vitamin C (mg):						
With supplements	70	113	154	229	705	
Adjusted for age	1·0	1·00	0·94	0·86	0·83	0·10
Multivariate model	1·0	1·10	1·08	1·01	0·98	0·60
(95% confidence interval)‡		(0·81 to 1·47)	(0·80 to 1·46)	(0·74 to 1·37)	(0·72 to 1·32)	
No supplements	61	94	120	152	209	
Adjusted for age	1·0	0·99	0·92	0·82	0·90	0·18
Multivariate model	1·0	1·12	1·10	1·03	1·16	0·76
(95% confidence interval)‡		(0·84 to 1·51)	(0·81 to 1·48)	(0·76 to 1·41)	(0·85 to 1·59)	
Vitamin E (mg‖):						
With supplements	3·3	4·4	5·7	17·1	209·8	
Adjusted for age	1·0	0·92	0·83	1·00	0·84	0·52
Multivariate model	1·0	1·00	0·97	1·10	0·96	0·88
(95% confidence interval)‡		(0·75 to 1·35)	(0·72 to 1·31)	(0·82 to 1·47)	(0·72 to 1·29)	
No supplements	3·2	4·0	4·7	5·4	6·9	
Adjusted for age	1·0	0·87	0·85	0·83	0·73	0·03
Multivariate model	1·0	0·95	0·95	1·01	0·88	0·40
(95% confidence interval)‡		(0·71 to 1·27)	(0·71 to 1·27)	(0·75 to 1·34)	(0·65 to 1·18)	
Antioxidant score:						
With supplements	6	9	12	15	18	
Adjusted for age	1·0	1·01	0·97	0·92	0·74	0·04
Multivariate model	1·0	1·02	0·93	1·03	0·76	0·09
(95% confidence interval)†		(0·75 to 1·37)	(0·73 to 1·19)	(0·72 to 1·49)	(0·57 to 1·03)	
No supplements	7	10	12	14	17	
Adjusted for age	1·0	0·75	0·84	0·74	0·57	<0·001
Multivariate model	1·0	0·80	0·87	0·78	0·60	0·002
(95% confidence interval)†		(0·59 to 1·09)	(0·65 to 1·16)	(0·59 to 1·02)	(0·45 to 0·81)	

*Adjusted in categories of five years.
†Each logistic model included terms for age (five year categories), time period (two year intervals), diabetes, energy intake (in fifths), smoking (never, past, current in four categories of use), Quetelet's index (<21, 21-<23, 23-<25, 25-<29, ≥29 kg/m^2), area of residence (north east USA, north central USA, California, Florida, Texas), number of physician visits (0, 1, 2, ≥3), and aspirin use (never, 1-6, 7-14, ≥15 tablets/week).
‡Including the variables above plus carotene.
‖ α Tocopherol equivalents.

experimental setting. Results using energy adjusted and non-adjusted nutrients were similar; therefore we present results only from the adjusted analysis. We calculated nutrient intake both including and excluding the contribution from vitamin supplements. For each participant, the quintile value for each nutrient was also summed and the sum recategorised by approximate quintiles to create an antioxidant score. Two scores were calculated: the first used carotene and vitamins E, C, and riboflavin without supplements, and the second score included supplements.

Incidence rates were calculated for each exposure category by dividing the number of cataract extractions by the person time of follow up for that category. Relative risks were used as the measure of association and were calculated as the ratio of incidence rates of exposed subjects to unexposed subjects. To control simultaneously for other potential risk factors we used proportional hazard models.[31 32] We calculated 95% confidence intervals and two sided p values for the Mantel extension test for trend.

TABLE II—*Age adjusted relative risk of cataract extraction by frequency of consumption of foods rich in carotenoids as assessed in 1980, 1982, and 1984*

Food	Frequency: <1 Time/ month	1-3 Times/ month	1 Time/ week	2-4 Times/ week	≥5 Times/ week	95% Confidence interval (highest *v* lowest category)	p Value for trend
Broccoli							
1980	1·0	0·91	1·07	0·81	0·78	(0·40 to 1·54)	0·53
1982	1·0	0·67	0·75	0·84	0·83	(0·37 to 1·84)	0·89
1984	1·0*		1·02	1·10†		(0·74 to 1·63)	0·67
Carrots							
1980	1·0	0·90	1·07	0·81	1·03	(0·64 to 1·66)	0·77
1982	1·0	0·96	0·77	0·75	0·86	(0·50 to 1·48)	0·16
1984	1·0	0·87	0·75	1·04	0·43	(0·17 to 1·09)	0·47
Spinach							
1980	1·0	0·70	0·81	0·69	0·53	(0·38 to 0·73)	0·001
1982	1·0	0·97	0·90	0·78	0·35	(0·16 to 0·77)	0·01
1984	1·0	1·04	0·77	0·62	0·51	(0·16 to 1·60)	0·02
Sweet potato							
1980	1·0	0·67	0·91‡			(0·62 to 1·33)	0·01
1982	1·0	0·91	0·79‡			(0·47 to 1·33)	0·16
1984	1·0	0·98	0·50‡			(0·24 to 1·06)	0·18
Winter squash							
1980	1·0	0·88	0·88	0·66†		(0·42 to 1·05)	0·05
1982	1·0	0·90	0·85	1·16†		(0·73 to 1·85)	0·73
1984	1·0	0·85	0·74‡			(0·47 to 1·15)	0·14

In 1980 there were 493 cataract extractions; in 1982, 365; in 1984, 170.
*≤3 Times a month. †≥2 Times a week. ‡≥1 Time a week.

TABLE III—*Relative risk of cataract extraction (n=493) according to duration of vitamin supplement use*

	Duration of use (years): 0	<2	2-4	5-9	≥10	p Value for trend
Multivitamins:						
No of cases	315	29	43	42	45	
No of person years	230 867	26 545	25 781	22 307	29 117	
Age adjusted relative risk	1·0	0·95*	1·29	1·30	0·93	0·53
Multivariate model (95% confidence interval)†	1·0	0·97 (0·66 to 1·42)	1·31 (0·95 to 1·81)	1·28 (0·92 to 1·79)	1·00 (0·74 to 1·38)	0·30
Vitamin A:						
No of cases	471	7	7	4	1	
No of person years	334 866	3893	3094	2906	2300	
Age adjusted relative risk	1·0	1·21	1·50	0·82	0·20	0·30
Multivariate model (95% confidence interval)†	1·0	1·12 (0·50 to 2·50)	1·64 (0·77 to 3·46)	0·89 (0·33 to 2·39)	0·23 (0·03 to 1·57)	0·44
Vitamin C:						
No of cases	397	22	25	22	13	
No of person years	282 846	13 924	15 298	15 558	12 716	
Age adjusted relative risk	1·0	1·08	1·05	0·83	0·50	0·03
Multivariate model (95% confidence interval)†	1·0	1·12 (0·73 to 1·73)	1·11 (0·74 to 1·67)	0·89 (0·58 to 1·37)	0·55 (0·32 to 0·96)	0·10
Vitamin E:						
No of cases	416	19	26	18	8	
No of person years	304 055	11 789	11 327	11 291	5580	
Age adjusted relative risk	1·0	1·03	1·27	0·83	0·64	0·51
Multivariate model (95% confidence interval)†	1·0	1·09 (0·69 to 1·73)	1·37 (0·92 to 2·04)	0·85 (0·52 to 1·38)	0·70 (0·35 to 1·41)	0·68

Total numbers of cases and person years vary owing to missing data.
*Adjusted for age in five year categories.
†Controlling for age, time period, diabetes, smoking, Quetelet's index, area of residence, and energy adjusted carotene intake in 1980.

TABLE IV—*Age adjusted relative risk of cataract extraction (n=493) by duration of vitamin C use within category of smoking*

Smoking (pack years)	Duration of vitamin C supplement use (years): 0	<2	2-4	5-9	≥10	p Value for trend
Never	1·0	1·22	1·00	0·87	0·27	0·06
1-44	1·0	1·25	0·69	0·74	0·72	0·22
≥45	1·0	0·68	2·00	1·07	0·72	0·78

Results

NUTRIENT INTAKE

Carotene, preformed vitamin A without supplements, and total vitamin A intake as assessed in 1980 were inversely associated with cataract extraction in analyses adjusted for age (table I). Vitamin C without supplements was unrelated to cataract extraction; vitamin C intake including supplements was weakly (and non-significantly) related to lower risk. For vitamin E and riboflavin, intake without supplements was inversely related to risk; however, no association was seen when the contribution from supplements was added.

We also assessed the relation between nutrient intake and cataract, controlling for several potential cataract risk factors: age, time period, smoking status, Quetelet's index, diagnosis of diabetes, energy intake, area of residence in 1976, aspirin use, and number of visits to a physician or clinic in 1978. Multivariate models were run first for each nutrient alone, next with the addition of carotene, and finally with all nutrients simultaneously. The estimates from the set of models with each nutrient plus carotene were similar but had narrower confidence limits than those from the model containing all nutrients and therefore are presented here. In these analyses, women in the highest fifth of carotene or total vitamin A intake had a 27-39% reduction in relative risk (table I). The inverse association with preformed vitamin A without supplements was weaker but remained significant. The relation with riboflavin without supplements was also weaker and the trend was not significant. None of the remaining associations were statistically significant.

Assessment of nutrient intake as reported in 1984 was limited by the smaller number of women (170) who had cataracts that had been extracted in 1984-8 but had not been diagnosed at the return of the 1984 questionnaire. The relative risk in the highest fifth of carotene intake was similar to that noted in 1980 analyses (relative risk 0·69 (0·43 to 1·09)), although the trend was not significant. Preformed vitamin A without supplements was most strongly associated with a decrease in cataract risk (relative risk for highest *v* lowest fifth 0·48 (0·29 to 0·78)) and an inverse association was noted for riboflavin without supplements (relative risk for highest *v* lowest fifth 0·61 (0·38 to 0·98)). Riboflavin with supplements, vitamin C, and vitamin E were not related to cataract extraction.

FOOD INTAKE

Because of the inverse association of cataract with carotene and total vitamin A intake as assessed in 1980 we assessed the association with individual foods containing carotene. No association was noted for carrots, the largest source of β carotene,[33] but a strong inverse association was seen for dietary intake of spinach and other greens (table II). Sweet potato and winter squash were weakly inversely associated with cataract. Similar relations were found with 1982 and 1984 data on diet, spinach being inversely associated with cataract and carrots having little relation to risk.

USE OF VITAMIN SUPPLEMENTS

Duration of use of multivitamin supplements (up to 1980) was not related to the risk of cataracts, but use of vitamin C supplement for ≥10 years was inversely related to cataract (relative risk 0·50 (0·29 to 0·87)) (table III). An inverse association with long term use of

TABLE V—*Age adjusted relative risk of cataract extraction by carotene intake within category of smoking*

Smoking (pack years)	Energy adjusted carotene intake (fifths) 1	2	3	4	5	p Value for trend
Never	1·0	0·97	0·55	0·62	0·61	0·003
1-44	1·0	1·13	0·96	0·58	0·74	0·02
≥45	1·0	1·26	1·15	0·96	0·98	0·60

specific vitamin A and E supplements was suggested, but the associations were not statistically significant. Results of the multivariate analysis were similar.

ANTIOXIDANT SCORE

In the multivariate analysis, women in the highest fifth of the antioxidant score excluding supplements had a 40% decrease in risk (table I). The inverse relation was weaker when vitamin supplements were considered (relative risk for highest *v* lowest fifth 0·76 (0·57 to 1·03)).

EFFECT MODIFICATION BY SMOKING

The inverse association between long term use of vitamin C supplement and cataract seemed strongest among never smokers, but the confidence intervals were wide (tables IV and V). Similarly, the inverse association noted between carotene and cataract seemed strongest among non-smokers, while little association was noted between carotene intake and cataract in those who smoked 45 packs a year or more. Adding interaction terms to a multivariate model, however, did not yield significant results.

Discussion

In this prospective study we found an inverse association between intake of several nutrients and extraction of cataracts. Carotene and total vitamin A without supplements were most strongly related to a decreased risk: women in the highest fifth of total vitamin A intake (excluding supplements) had a 40% lower risk of cataract extraction relative to those in the lowest fifth. Little relation was noted between vitamins C or E or riboflavin from food sources and cataract extraction, but long term users of vitamin C supplement had a lower risk. The antioxidant score without supplements also was associated with a 40% reduction in risk for women in the highest fifth of intake.

Stronger associations were generally seen among the nutrient scores that excluded supplements. Nutrient intake calculated without supplements may better reflect long term intake because women who began using supplements just before completing the questionnaire would be classified in the highest fifth of intake regardless of their intake in the more distant past. Also, nutrients in the foods other than those in the vitamin supplements may also influence risk.

Carrots, the richest source of β carotene, were not related to cataract extraction but spinach was consistently associated with a decreased risk. Perhaps a carotenoid other than β carotene is influencing risk: according to preliminary nutrient tables compiled by the United States Department of Agriculture, spinach is high in lutein and zeaxanthin and carrots are low in these carotenoids. These findings regarding different sources and forms of carotenoids should be considered speculative and preliminary and require confirmation.

In 1980, the inverse association between intake of preformed vitamin A without supplements and cataract was somewhat weaker than the association noted with carotene, but the opposite was found from the 1984 data. Preformed vitamin A may have an independent role in preventing cataract, or it might influence the risk of cataract through its relation with carotene; it has been suggested that people with ample intakes of preformed vitamin A might convert less carotene to retinol, thus sparing plasma carotene.[34]

Long term users of vitamin C supplement had a substantial decrease in risk, yet no association was seen with long term use of multivitamins. Most of the multivitamin preparations available in the United States contained 60-90 mg of vitamin C (up to 1·5 times the recommended daily allowance), and the vitamin C supplements most often contained 250-500 mg; if the protective effect is real, higher doses of vitamin C seem to be needed to afford protection. Relatively few women were long term users of vitamins E or A; longer follow up will be needed before dismissing a possible influence of these vitamins on risk of cataracts.

Cigarette smoking is associated with increased lipid peroxidation,[35] low plasma antioxidant levels,[34 36] and an increased risk of cataract[37 38]; thus we hypothesised that the association between cataract risk and both carotene and vitamin C supplement use might vary by smoking status. The protective effect of carotene and vitamin C supplement use seemed to be greatest among never smokers, but interaction terms added to a multivariate model were not statistically significant.

Because repeatedly examining this large cohort in a standardised manner was not possible, the procedure of cataract extraction was used to define the occurrence of disease; in this way we were unlikely to include false positive cases. Although there were women with cataracts not requiring extraction among women not included among the cases, underascertaining cases, if not associated with exposure, does not bias the relative risk in a cohort study.[39] In addition, the cataracts in this study were those sufficiently severe to affect vision and therefore of greatest clinical and public health importance.

This use of cataract extraction, rather than cataract not yet requiring surgery, also decreases the chance for variation in the thresholds for diagnosis of disease. Because all subjects are nurses, their access to medical care and their threshold for surgery are likely to be more uniform than in the general population. In 1990, over 80% of respondents reported having had an eye examination in the previous two years. Nevertheless, if nurses who were more health conscious and likely to consume vitamins also tended to have cataracts extracted at either an earlier or later stage, relative risks would have been biased. To examine this we assessed the Spearman correlation between each nutrient and the visual acuity before surgery in the eye being operated on as an index of disease severity. These correlations were all very small (range $-0·11$ to 0·08). Also, controlling for the number of visits to a physician in 1978 did not alter the coefficients found for nutrients in a multivariate model. Finally, women in the highest fifth of intake for each nutrient were just 2-5% more likely to be examined by an eye doctor from 1988-90 than were women in the lowest fifth. Therefore, any bias from using cataract extraction as the end point is likely to have been minimal in this study.

Data on exposure were collected before diagnosis, thus, any misclassification would be unrelated to risk of cataract and would tend to bias our associations towards the null. The high follow up rate in this cohort, 96% in 1988 as a percentage of total possible follow up time, minimises this as a source of bias. Although we controlled for several cataract risk factors in the analysis (age, diabetes, smoking), the effect of unmeasured risk factors is always a concern and may have distorted the associations seen with diet. We were unable to control for the effects of exposure to sunlight although such variation is not likely to be large because the cohort is not occupationally exposed.

Inverse associations between cataract and plasma[16] or dietary carotene,[19] and total vitamin A[19] have been reported in some but not all studies.[22] A decrease in risk has also been reported among consumers of ≥3·5 servings of fruits and vegetables daily.[17] Associations with specific foods were not presented in these studies. Conflicting results were found in two studies of plasma vitamin C and cataract,[16 24] perhaps because plasma concentrations reflect only recent intake.[40] With one exception,[19] no association has been reported between cataracts and dietary vitamin C[19 22 23] or vitamin E,[17 19 22] findings similar to ours. Conflicting results also have been reported for the association between riboflavin and cataract.[16 19-22 24]

Robertson *et al* reported a 70% reduction in cataract among subjects who used specific vitamin C supplements over five years and a 55% reduction in risk among vitamin E users.[18] The risk reduction associated with vitamin C use was somewhat greater than that which we found among long term users. We found no significant reduction in cataract risk among users of vitamin E supplements, but our analysis was limited by the small number of women who used these supplements. Leske *et al* reported a 40% decrease in risk of cataract among users of multivitamin supplements,[19] but Robertson *et al* found no such association.[18]

Most[19 24 41] but not all[22] studies that have computed antioxidant indexes similar to ours have found an inverse association with cataract. Although the magnitude of the protection varied, the overall consistency lends some support to the hypothesis that antioxidants may decrease the risk of cataracts and that there may be a cumulative effect in their ability to do so.

Vitamin C has been found in relatively high concentrations in the lens,[14] and these concentrations increase with vitamin C supplementation.[42] Vitamin E is found in the human lens; in rats, concentrations in the lens do not increase with dietary supplementation,[43] but this has not been studied in humans. Although riboflavin deficiency results in cataracts in animals,[6-8] the effect of supplementation has not been assessed. The effect of carotenoids has not been assessed in animal or in vitro experiments. The antioxidant activity of β carotene is well established, and other carotenoids are also effective antioxidants[44 45] and may serve that function in the lens.

Our findings suggest that dietary carotenoids, although not necessarily β carotene, and long term use of vitamin C supplements may lower the incidence of cataracts severe enough to require extraction. These findings lend support to the antioxidant hypothesis of cataract prevention. Confirmation and further examination of these complex relations in other data sets is needed.

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