Long-term vitamin C supplement use and prevalence of early age-related lens opacities


ABSTRACT We designed the present study to examine the cross-sectional relation between age-related lens opacities and vitamin C supplement use over a 10–12-y period before assessment of lens status in women without diagnosed cataract or diabetes. This design avoids biased measurement of nutrient intake that results when knowledge of lens opacities influences nutrition-related behavior or its reporting. The participants were 247 Boston-area women aged 56–71 y selected from the Nurses’ Health Study cohort with oversampling of women with high or low vitamin C intakes. Lens opacities were graded with the Lens Opacification Classification System II. Use of vitamin C supplements for ≥10 y (n = 26) was associated with a 77% lower prevalence of early lens opacities (odds ratio: 0.23; 95% CI: 0.09, 0.60) at any lens site and a 83% lower prevalence of moderate lens opacities (odds ratio: 0.17; 95% CI: 0.03, 0.85) at any lens site compared with women who did not use vitamin C supplements (n = 141) after adjustment for age and other potentially confounding variables. Women who consumed vitamin C supplements for <10 y showed no evidence of a reduced prevalence of early opacities. These data, together with data from earlier experimental and epidemiologic studies, suggest that long-term consumption of vitamin C supplements may substantially reduce the development of age-related lens opacities. Am J Clin Nutr 1997;66: 911–6.

KEY WORDS Cataracts, vitamin C, women, lens opacities, aging, antioxidants

INTRODUCTION

Because oxidation of lens proteins appears to play a central role in the formation of age-related cataracts (1, 2), research regarding the etiology of cataracts has focused on the role of dietary antioxidants (ie, vitamins C and E and carotenoids). Evidence from cell-free, in vitro, and animal experiments supports the hypothesis that these antioxidants can delay the onset of age-related lens changes (1, 2). This experimental laboratory evidence has prompted epidemiologic investigations of the relation between antioxidant nutrients and risk of cataract (3–13). In several of these studies a lower risk of cataract was seen in individuals with high blood concentrations or intakes of vitamin C (3, 4, 6, 9, 10), vitamin E (3, 4, 6, 8, 11), carotenoids, or vitamin A (3, 6, 10, 11). Cataract risk was also reported to be lower in individuals who consume multivitamin supplements (9, 12, 13).

With one exception (10), the epidemiologic studies relating vitamin C to risk of cataract or cataract extraction are based on concurrent or past measures of nutrient status or intake. Concurrent assessment of lens opacification and vitamin C intake or status may result in a biased association if knowledge of opacities influences nutrition-related behavior or its reporting. We designed the present study to examine the relation between prevalence of age-related lens opacities in women who were free of diagnosed cataract and long-term vitamin C intake. To do this we used information on vitamin C supplement use measured five times over a 10–12-y period before assessment of lens status. We chose to focus on vitamin C because 1) experimental evidence indicates that vitamin C can protect lens constituents against oxidation in vivo and in vitro (1, 2), human lenses concentrate vitamin C against a strong concentration gradient (14), 3) lens vitamin C concentrations respond to dietary manipulation (14), and 4) long-term vitamin C supplement use was associated with a lower rate of cataract extraction in a previous analysis in the Nurses’ Health Study (10).

SUBJECTS AND METHODS

Subjects

In 1976, 121 700 female nurses aged 30–55 y who resided in 11 US states completed a mailed questionnaire on known and

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suspected risk factors for cancer and heart disease. These women formed the Nurses’ Health Study (NHS) cohort (15). Every 2 y since 1976, these women have been contacted by mail to update information on risk factors and disease status.

We identified 2484 NHS cohort members aged 55–69 y in 1990 without cancer other than nonmelanoma skin cancer who resided in eastern Massachusetts. Our goal was to enroll 300 women. To achieve sufficient statistical power to examine the hypothesis that vitamin C intake is associated with cataract risk for a sample of this size, it was necessary to enrich our sample with women who had high and low vitamin C intakes. We ranked the eligible members of this subcohort according to their vitamin C intakes using information on total vitamin C intake (dietary plus supplemental) from the 1980 and 1984 NHS food-frequency questionnaires and vitamin C supplement use from the 1986 questionnaire. (Although dietary data were also collected on the 1986 questionnaire, these data were not available at the time we identified our study sample.) If a woman was in the higher intake deciles in either 1980 or 1984 or if supplemental vitamin C use was reported in 1986, she was eligible for inclusion in a “high” intake group. If a woman’s intake was in the lower deciles in 1980 or 1984 and she did not report vitamin C supplement use in 1986, she was eligible for inclusion in a “low” intake group. Women who had intakes in the higher deciles in either 1980 or 1984 and in the lower deciles in the alternate year were not eligible for either group. Between 1990 and 1992, we invited eligible women with the highest and lowest intakes to participate in a detailed eye examination. To meet our recruitment goals, we had to continually modify the criteria for inclusion in the high and low intake groups by decreasing and increasing the intake decile cutoffs, respectively.

Potential participants were initially contacted by a letter from the NHS and requested to return an enclosed reply postcard indicating whether or not they would be willing to participate in the study. To preserve their participation in the NHS, women who did not return the postcard received no further mailings or phone contact. Starting with the women in the highest intake deciles and working down, and those in the lowest intake deciles and working up, we invited 1051 women to participate. Our final sample consisted of 301 women (29% of those invited), 165 with a high and 136 with a low vitamin C intake. The low response rate was largely due to the failure of women to respond to the one mailed invitation and the lack of follow-up contact for women who did not return their reply postcards. Informed consent was obtained from all study participants and all procedures were approved by the Human Investigations Review Committee at the New England Medical Center and the Human Research Committee at Brigham and Women’s Hospital.

Assessment of nutrient intake

A 61-item semiquantitative food-frequency questionnaire was initially incorporated as part of the NHS in 1980 (16). This questionnaire queried usual intake over the previous year with nine possible response categories ranging from “never or less than once per month” to “six or more times per day.” In addition to information on food intake, the food-frequency questionnaire also collected information on vitamin supplement use in 1980 and duration of vitamin supplement use before 1980. In 1984 and again in 1986, the food-frequency questionnaire was revised and expanded to include ~130 food items and details of vitamin and mineral supplement use that collectively account for >90% of the total absolute intake of the 70 nutritional indexes measured by this instrument (17). The food-frequency questionnaire has been validated extensively relative to both long-term diet records (16, 17) and biochemical markers of nutrient status (18–20). Information on vitamin supplement use was requested of NHS participants on other questionnaires in the biennial cycles in which food-frequency questionnaires were not collected (1982 and 1988).

We used five reports of vitamin supplement use from the 1980 through 1988 biennial questionnaires to characterize vitamin C supplement use. We categorized women by duration of vitamin C supplement use (excluding intake from multivitamin supplements), which was determined as the reported duration of use before 1980 plus two additional years for each report of supplement use on the biennial questionnaires from 1980 to 1988. Women who did not report supplement use on any of the biennial questionnaires between 1980 and 1988 were classified as nonusers. Women with incomplete supplement data were included in the analyses of supplement data if they did not have missing data from consecutive biennial questionnaires and reported use was the same before and after the period for which the data were missing. In this case (n = 2), we assumed that supplement use was similar at the intermediate (missing) time period.

Our method of sampling resulted in a situation in which usual vitamin C intake and vitamin C supplement use were intimately linked: 70% of the women with high vitamin C intakes used vitamin C supplements and an additional 22% of the women with high vitamin C intakes used multivitamins. Therefore, we limited these analyses to information on vitamin C supplement use. We did not consider dietary vitamin C intake separately. Our sampling scheme did not limit the variability of other nutrients, but it did not provide acceptable statistical power to adequately consider relations between dietary or supplemental intake of other nutrients and lens opacification.

Assessment of lens status

All participants received a detailed eye examination. The examiner had no knowledge regarding the nutrient status of any of the volunteers. The examination included an ocular history, visual acuity and manifest refraction, external ocular examination, applanation tonometry, and a slit-lamp examination of the anterior segment, including assessment of the anterior chamber to determine risk of angle-closure glaucoma. The pupils were then dilated with 1% tropicamide and 2.5% neosynephrine (both from Alcon, Fort Worth, TX) to a minimum of 7 mm before the lens was examined with a slit lamp. The posterior segment was examined by direct and indirect ophthalmoscopy and slit-lamp biomicroscopy. Presence and degree of lens opacification were classified by a single examiner (ML) using the Lens Opacities Classification System (LOCS) II clinical grading protocol at the slit lamp, with the LOCS II standards hung beside the head of the volunteer (21). This protocol assesses features of nuclear opalescence (with five possible grades), cortical opacity (with seven possible grades), and posterior subcapsular opacity (with five possible grades). LOCS II was designed and validated to grade lens opacities at the slit lamp or to grade slit-lamp and retroillumination pho-
to graphs. Grading at the slit lamp with LOCS II is highly reproducible and shows good agreement with photographic classifications (21). LOCS grading was repeated by a second examiner in 30% of participants to monitor reproducibility. Agreement between the two examiners was 97%. For these analyses, we classified women based on location and degree of opacification in the worst eye: women with opacity grades ≥ 2 at a particular site in either lens were defined to have moderate opacities; women with opacity grades ≥ 1 and < 2 in either lens were defined to have early opacities, and women with opacity grades < 1 were considered to have clear lenses at that site.

Nonnutritional risk factors

Data on known or suspected nonnutritional determinants of cataract risk were obtained from the 1980 through 1988 biennial NHS questionnaires. For the present analyses, we considered confirmed history of diabetes (yes or no) as reported on the 1988 or previous questionnaires; pack-years smoked through 1990; reported summertime sunlight exposure (≥ 8 h/wk) as reported on the 1980 questionnaire; regular aspirin use as reported on the 1980, 1982, and 1984 questionnaires; postmenopausal hormone use through 1990; and height and weight as reported on the 1980 questionnaire. The latter two measures were used to calculate body mass index (wt in kg/m² in m). Pack-years smoked were divided into three categories: never smoked, 1–29 pack-years, and ≥ 30 pack-years. Use of postmenopausal hormones was categorized as either never, past (use before 1990), or current (use in 1990). Presence of age-related maculopathy, defined as a maculopathy grade ≥ 1 according to the classification procedure of Bressler et al (22), was ascertained at the time of the ocular examination.

Statistical analyses

We used polytomous logistic regression to estimate the odds ratios (ORs) relating prevalence of early and moderate opacities to duration of vitamin C supplement use. All ORs were adjusted for age and other potential confounders, including pack-years smoked, body mass index, reported summertime sunlight exposure, aspirin use, postmenopausal hormone therapy, and presence of age-related maculopathy. Categories of duration of vitamin C supplement use were modeled with indicator variables by using women who reported no vitamin C supplement use as the reference category. The ORs and 95% CIs for each supplement-use duration category were determined as the antilogarithms of the corresponding logistic-regression coefficient and the regression coefficient ± 1.96 times the SE of the coefficient. [We used exact procedures to estimate age-adjusted CIs when the number of women within the supplement-use duration categories was zero (23)]. We examined relations between duration of vitamin C supplement use and the presence of any opacity (ie, opacities at any site in the lens) and nuclear opacities. There were too few women with posterior subcapsular and cortical opacities to consider these sites separately. P values for trend across duration categories were determined from polytomous logistic-regression models with duration of vitamin C supplement use entered in its continuous form. All models that we used in these analyses met the criteria for appropriate goodness of fit (24). Logistic-regression analyses were performed with the SYSTAT LOGIT module (25).

RESULTS

Characteristics of eligible women who were not invited to participate and of the invited women who did and did not participate in the study are compared in Table 1. The only notable difference between women who were invited and those who were not invited was seen for vitamin C intake and multivitamin and vitamin C supplement use. These differences would be expected based on the sampling scheme because women with low and high vitamin C intakes were oversampled. The proportion of women with a history of cataract was essentially the same in women who were invited and those who were not. Of the women who were invited, those who participated were less likely than invited nonparticipants to be current smokers (by 10%) and more likely to be aged ≥ 65 y (by 8%) than women who did not participate. Participants were slightly more likely than invited nonparticipants (by 4%) to be in the highest vitamin C intake quintile in 1980 and a larger percentage of participants than nonparticipants fell into the high vitamin C group (by 7%), but participants and invited nonparticipants were similar with respect to vitamin C supplement use through 1988 and history of cataract. Invited participants within the high- and low-vitamin C groups had prevalences of previous cataract diagnosis and vitamin C supplement

### TABLE 1

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Not invited (n = 1433)</th>
<th>Nonparticipants (n = 750)</th>
<th>Participants (n = 301)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, 1990</td>
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<td></td>
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<tr>
<td>55–59 y</td>
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<tr>
<td>60–64 y</td>
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<td></td>
<td></td>
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<tr>
<td>65–69 y</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Smoking status, 1988</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Never</td>
<td>34</td>
<td>37</td>
<td>32</td>
</tr>
<tr>
<td>Past</td>
<td>35</td>
<td>35</td>
<td>33</td>
</tr>
<tr>
<td>Current</td>
<td>31</td>
<td>28</td>
<td>36</td>
</tr>
<tr>
<td>History of cataract, 1990 or earlier</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td></td>
<td>13</td>
<td>11</td>
<td>12</td>
</tr>
<tr>
<td>History of diabetes, 1988 or earlier</td>
<td></td>
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<td></td>
</tr>
<tr>
<td></td>
<td>7</td>
<td>5</td>
<td>3</td>
</tr>
<tr>
<td>Vitamin C intake quintiles, 1980²</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>&lt; 93 mg</td>
<td>10</td>
<td>21</td>
<td>23</td>
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<tr>
<td>93–131 mg</td>
<td>23</td>
<td>23</td>
<td>19</td>
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<tr>
<td>132–182 mg</td>
<td>33</td>
<td>16</td>
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<tr>
<td>183–358 mg</td>
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<td>22</td>
</tr>
<tr>
<td>≥ 359 mg</td>
<td>7</td>
<td>18</td>
<td>22</td>
</tr>
<tr>
<td>Vitamin C supplement use, 1988 or earlier</td>
<td></td>
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<td></td>
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<tr>
<td></td>
<td>20</td>
<td>38</td>
<td>40</td>
</tr>
<tr>
<td>Multivitamin supplement use, 1988 or earlier</td>
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<td></td>
</tr>
<tr>
<td></td>
<td>48</td>
<td>58</td>
<td>62</td>
</tr>
<tr>
<td>Initial vitamin C intake group³</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>High</td>
<td></td>
<td>48</td>
<td>55</td>
</tr>
<tr>
<td>Low</td>
<td></td>
<td>52</td>
<td>45</td>
</tr>
</tbody>
</table>

¹ In some cases percentages do not add up to 100 because of rounding.
² Energy-adjusted vitamin C intake quintiles based on entire cohort with intake data available in 1980.
³ Based on total intake in 1980 and 1984 and supplement use in 1986.
use similar to those of the nonparticipants in the respective vitamin C groups (data not shown).

Of the 301 women examined, we excluded 7 women from the analysis because they did not have two intact lenses and 42 women who reported a history of cataract at their study eye examination to avoid the possibility that prior knowledge of lens opacification might influence vitamin C supplement use. We excluded an additional five women with a confirmed diagnosis of diabetes in 1988 or earlier because the combination of their small number and the high correlation between diabetes and lens opacification interfered with the convergence of the logistic-regression models. Consequently, 247 women were included in these analyses.

At the time of their eye examinations (1990–1992) the mean age of this sample of women was 62.6 y (range: 56–71 y); 27% were aged < 60 y, 37% were aged 60–64 y, and 36% were aged ≥ 65 y. Thirty-seven percent of these women never smoked, and 30% and 32% accumulated 1–29 and ≥ 30 pack-years, respectively. Twenty-five percent of the women had reported postmenopausal hormone use before 1990 but not in 1990 (past use), and 19% reported use of hormones in 1990 (current use). Eleven percent had a diagnosis of age-related maculopathy based on their ocular examination. Eighty-three percent reported summertime sunlight exposure of ≥ 8 h/wk and 21% reported regular aspirin use. Mean body mass index was 24.3. Vitamin C supplement use was reported by 42% of our sample during the period between 1980 and 1988. Thirteen percent of the women reported taking vitamin C supplements for 1–4 y, 18% for 5–9 y, and 11% for ≥ 10 y as of 1988. Of the 26 women who took supplements for ≥ 10 y, 4 had an average dosage of < 400 mg/d, 12 an average dosage of 400–700 mg/d, and 10 an average dosage of > 700 mg/d.

Of the 247 women with complete lens data, 59 (24%) had clear lenses, 156 (63%) had early opacities (ie, LOCS II grade 1), and 32 (13%) had moderate opacities (ie, LOCS II grade ≥ 2). Most of the opacities were found in the nuclear region of the lens. Sixty-one percent of women had early nuclear opacities and 12% had moderate nuclear opacities. Early and moderate cortical opacities were seen in 9% and 4% of women studied, respectively. Four percent had early posterior subcapsular opacities whereas none of these women had moderate opacities at this site. Because of the small numbers of women with cortical and posterior subcapsular opacities, these two sites were not considered separately in this report.

The relation between duration of vitamin C supplement use and risk of lens opacification is shown in Table 3. Use of vitamin C supplements for ≥ 10 y was associated with a substantially lower prevalence of both early (OR: 0.23; 95% CI: 0.09, 0.60) and moderate (OR: 0.17; 95% CI: 0.03, 0.87) opacities at any lens location after adjustment for potentially confounding variables. Similarly, the prevalence of early nuclear opacities was significantly lower among women who consumed vitamin C supplements for ≥ 10 y (OR: 0.22; 95% CI: 0.09, 0.56), and none of the 26 women who took supplements for ≥ 10 y had moderate nuclear cataracts. The age-adjusted exact 95% CI for the ORs of moderate nuclear cataracts was 0.00, 0.47. Although the tests for trend across duration categories were significant for early and moderate grades of any type of opacity, there was little evidence that women who used vitamin C supplements for < 10 y had a lower prevalence of early opacities. These associations were not influenced by adjustment for either vitamin E or carotene intakes (including diet plus supplements) or multivitamin supplement use.

**DISCUSSION**

The NHS nutritional data provided us with the opportunity to use multiple measures of vitamin C supplement use collected prospectively over 10–12 y before eye examinations to determine whether elevated vitamin C intake for more than a decade was related to a lower risk of ocular lens opacities. In this study we observed a > 75% lower prevalence of lens opacification, most notably in the nuclear region, in women aged 56–71 y who used vitamin C supplements for ≥ 10 y. This association was not affected by adjustment for other antioxidant nutrients or nonnutritional factors that are believed to influence risk of opacification (1). These data corroborate the prior observation that long-term use of vitamin C supplements was associated with a 45% lower rate of lens extraction in the larger cohort from which our sample was derived (10). These data also suggest a lower prevalence of moderate opacities (ie, LOCS II grade ≥ 2) for women who used vitamin C supplements for < 10 y, although the ORs were not reduced significantly. Use of vitamin supplements for a period < 10 y was not associated with a lower prevalence of early opacities (ie, LOCS II grade 1).

Previous epidemiologic studies of age-related cataracts have also suggested a protective role of vitamin C. Of eight published studies that considered either vitamin C status or intake (3–10), five showed inverse associations between vitamin C and at least one measure of cataract (3, 4, 6, 9, 10), two observed no association (7, 8), and two reported positive associations (5, 9). Although the study of Mohan et al (5) suggested an increased risk of cataract with increasing plasma vitamin C, they showed a significantly reduced risk of cataract with increasing antioxidant scores that had plasma vitamin C as one of the antioxidant components. With one exception, these observations were based on assessment of nutrient intake or blood concentration at one time point, most often measured concurrently with lens status. It is possible that classification of nutrient intake or status at a single point in time might be insufficient to adequately characterize usual intake over the relevant period for development of lens opacities. The observed inconsistencies across these studies might result in part from misclassification of nutrient exposures.

The Linxian (China) intervention trials (13) provided the first data on the effect of antioxidant supplementation on cat-
<table>
<thead>
<tr>
<th>Duration of supplement</th>
<th>Any Grade &lt; 1</th>
<th>Grade 1 (Early)</th>
<th>Grade ≥ 2 (Moderate)</th>
<th>Nuclear Grade &lt; 1</th>
<th>Grade 1 (Early)</th>
<th>Grade ≥ 2 (Moderate)</th>
</tr>
</thead>
<tbody>
<tr>
<td>None</td>
<td>28</td>
<td>89</td>
<td>24</td>
<td>32</td>
<td>87</td>
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<tr>
<td>1-4 y</td>
<td>5</td>
<td>25</td>
<td>3</td>
<td>5</td>
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<td>3</td>
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<tr>
<td>5-9 y</td>
<td>10</td>
<td>30</td>
<td>3</td>
<td>14</td>
<td>27</td>
<td>2</td>
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<td>≥ 10 y</td>
<td>14</td>
<td>10</td>
<td>2</td>
<td>16</td>
<td>10</td>
<td>0*</td>
</tr>
<tr>
<td>P trend</td>
<td>0.02</td>
<td>0.03</td>
<td>0.003</td>
<td>0.004</td>
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</tr>
</tbody>
</table>

1 ORs for those women who took vitamin C supplements as compared with women who did not report taking vitamin C supplements were adjusted for age, pack-years of smoking, body mass index, reported summer-timers sunlight exposure, aspirin use, postmenopausal hormone use, and presence of age-related maculopathy; 243 women had complete data on lens status and all covariates. Median average (data from 3 FFQs) intake in nonsupplemented group was 130 mg/d.
3 Referent group.
4 No women who consumed vitamin C supplements for ≥ 10 y had moderate nuclear opacities; age-adjusted exact CIs.

The relatively low participation rate does not appear to have introduced any misrepresentation (or selection) bias in the present study. As part of the larger NHS, data on history of cataract and vitamin C supplement use were available for both participants, and prevalence of cataract history and vitamin C supplement use was similar in participants and invited nonparticipants. Moreover, we showed that prevalence of cataract and vitamin C supplement use among participants in the high and low vitamin C intake groups was nearly identical to that among invited nonparticipants in these groups. For bias to be present, participation would have to vary jointly by both vitamin C supplement use and lens status, which it did not. A notable difference between participants and nonparticipants was the proportion of current cigarette smokers. However, in the analyses we accounted for cigarette smoking, thus minimizing any potential bias. In addition, exclusion of current smokers from these analyses (data not shown) had little influence on the relation between vitamin C supplement use and prevalence of cataract at the time of the examination. Given that the early nature of the majority of lens opacities observed in the remaining women would not affect visual acuity, it was very unlikely...
that any of these women had any knowledge of their lens status. It is also possible that bias could have resulted from misclassification of lens opacity, but this would only reduce the observed strength of any association with vitamin C intake. Furthermore, the high reproducibility of the LOCS II assessment in this study would suggest that substantial misclassification was improbable.

Exclusion of women with previously diagnosed cataracts also removed another source of bias because women with a history of cataract were much more likely to start using vitamin C supplements during the interval of nutritional assessment (1980–1988) than were women without a history of cataract. This suggests that they started supplement use as a result of their diagnosis, possibly at the recommendation of their ophthalmologists, who may have been aware of ongoing research on vitamins and cataract. In 1980 there was little information regarding associations between risk for cataract and nutrition in humans. At that time, 19% of women with a history of cataract used vitamin C supplements compared with 18% of women without a history of cataract. By 1988, when reports regarding associations between nutrient intake and risk for cataract appeared, 57% of nurses with a history of cataract used vitamin C supplements whereas only 27% of women without a history of cataract used vitamin C supplements. Thus, inclusion of women with a prior diagnosis biases the relation between short-term supplement use and lens opacities, resulting in an apparent increased prevalence of opacities among short-term users of vitamin C supplements.

These data, together with results from experimental studies and previous epidemiologic findings for cataract extraction, suggest that long-term consumption of high amounts of vitamin C (in the present case primarily through dietary supplements) may substantially reduce the development of age-related lens opacities. These observations suggest that future studies of vitamin C and lens opacities, whether observational studies or supplementation trials, should be designed to measure intake or intervene with supplements for a period ≥ 10 y. Shorter periods might result in failure to observe any beneficial effects of vitamin C on cataract risk.

We are indebted to the nurses who participated in the study for their continuing contributions and cooperation; to Frank E Speizer, overall principal investigator for the Nurses’ Health Study for his support; and to Karen Corsano and Kate Saunders for their unfailing assistance.

REFERENCES