The importance of age-related cataract as a cause of worldwide blindness has led to many efforts to identify risk factors. Such studies have suggested a multifactorial etiology in cataractogenesis. Besides older age, consistent factors associated with all cataract types have been a lower level of education or a lower occupational status. In addition, the possible role of nutritional factors in cataractogenesis was suggested from evidence found in laboratory research. Various epidemiological studies have subsequently related the intake of some form of nutritional supplements or antioxidant nutrient status to a decreased risk of cataract. Socioeconomic status could be related to cataract risk through its influence on lifestyle behaviours, including dietary intake patterns. Similarly, the association between nutritional supplement use and cataract could be confounded by socioeconomic status. While the interrelationship of these variables cannot be easily clarified by observational epidemiological studies, population-based studies are less susceptible to selection and other biases. This report uses population-based data from the Barbados Eye Study (BES) to determine whether nutritional supplementation is related to age-related lens opacities in the black BES population, while controlling for potentially confounding variables. The associations with potentially modifiable factors indicate the need for further evaluations, given the high prevalence of lens opacities.
METHODS

The Barbados Eye Study

The BES was an epidemiological study to determine prevalence and risk factors for major eye diseases in the predominantly black population of Barbados. The study included 4709 Barbados residents, identified by a simple random sample of Barbadian-born citizens, between 40 and 84 years of age. The participation rate was 84%. Comprehensive ocular and other data were collected according to standardized methods and procedures, as described previously. Demographic information included age, sex, self-reported race, years of education of the participants and of their spouses, if any, major type of occupation, marital status and religion. Information collected on nutritional supplements included: use on a regular basis (at least once a week for at least one month), name of supplement and duration of use.

The lens was examined at the slit lamp under maximum dilatation with tropicamide. The Lens Opacities Classification System II (LOCS II) was used to grade opacities into five nuclear, five posterior subcapsular (PSC) and seven cortical ordinal grades of increasing severity, following photographic standards. After training and establishing baseline standardization, the reproducibility of LOCS II gradings among three examiners was evaluated throughout the BES data collection period and excellent reproducibility was achieved.

Definitions of Lens Opacities

The prevalence and distribution of all types of lens opacities in the BES were described elsewhere. The present report is based on age-related lens opacities among the 4314 black participants examined at the study site. The following definitions were used.

All lens changes. This broad definition included: (a) any type of gradable lens opacities, or, (b) history of prior cataract surgery, or, (c) cataract that was too advanced to grade (such as hypermature cataract). Overall, 1800 people had lens changes. To evaluate associations with all types of age-related opacities, analyses were based on this group.

Lens opacities by type. These were defined as a LOCS II score of two or more in either eye. Participants were considered to have a single type of opacity, i.e. nuclear only, cortical only or posterior subcapsular (PSC) only, if that was the sole type (with a score of ≥2) present in the individual. (In participants with unilateral cataract surgery or a non-gradable lens, the LOCS II gradings from the fellow eyes were used to classify types of lens opacities.) Among the BES black participants, 229 had nuclear opacities only, 851 had cortical opacities only, 17 had PSC opacities only, and 548 had mixed opacities, i.e. more than one type. To evaluate associations with specific types of lens opacities, the main analyses were based on participants with nuclear only and cortical only opacities, rather than on those with mixed opacities; they exclude those with PSC only opacities because of their small number.

No opacities. Participants were considered as having no opacities if their LOCS II scores were all under two for cortical, nuclear and PSC zones of the lens. These 2431 people served as the reference group when evaluating associations with all lens changes, or with nuclear only or cortical only opacities.

Risk factor analyses. The factors investigated in this report included age and sex; educational and occupational status, including an index of socioeconomic status (low: education ≤9 years for participant or spouse and a non-professional lifetime occupation [e.g. service, agricultural, production]; high: education >9 years and professional lifetime occupation [e.g. managerial, technical]; medium: otherwise); and regular intake of nutritional supplements (as defined earlier) that began at least a year prior to the interview. Logistic regression analyses were used to evaluate the associations of nutritional supplements with each of the lens status categories, i.e. all lens changes, nuclear only and cortical only opacities. These analyses controlled for socioeconomic status and other potential confounding factors, such as diabetes (self-reported history: yes versus no), obesity (waist-hip ratio: high, medium, low), hypertension (diastolic blood pressure >95mmHg: yes versus no), and smoking status (smoking in the past year: yes versus no). The results are presented as odds ratios (OR) and 95% confidence intervals (CI).

RESULTS

Table 1 presents demographic distributions by study group. The average age among participants with lens changes was 68.2 years, as compared to 51.8 years for those without lens opacities. Participants with nuclear opacities were older (70.2 years) than those with cortical opacities (64.2 years). The differences in the percentage of those widowed among the groups reflect their differences in age. The groups with lens opacities had more women, less years of education, and a higher frequency of a lifetime non-professional occupation than those without lens opacities. Religious backgrounds were similar among the study groups.
As seen in Table 2, people free of opacities used more nutritional supplements on a regular basis than those with opacities. When considering any type of regular supplement use, the frequency was 24.2% for the group with no opacities and lower for the groups with all lens changes (15.7%), nuclear only (14.9%) or cortical only opacities (16.5%). Similar results were found for longer duration of supplement use, i.e. for >2 years or >5 years. Cod liver oil and multivitamins were the most common types of supplements used in the BES population, while the regular intake of individual vitamin supplements was very infrequent.

The patterns of regular use of nutritional supplements in each study group, according to demographic characteristics, were further explored in Table 3. Supplement use was generally more frequent at younger ages, in females, in those with higher education levels and in those with professional occupations. Participants with all lens changes, or with nuclear only or cortical only opacities consistently used less nutritional supplements than others in every demographic category, with few exceptions. The exceptions were seen in the oldest age group, where those with nuclear and cortical opacities had somewhat higher supplement use, and in the higher educational status group, where those with nuclear opacities had similar frequency of use to those without opacities. These patterns were similar both for regular use of cod liver oil and of multivitamin supplements (data not shown).

Table 4 shows the results of multiple logistic regression analyses. Older age, as expected, was positively associated with all types of lens changes. Women had more lens changes than men (OR = 1.39) and in particular, more cortical opacities, (OR = 1.41). Lower SES, indicating both a lower educational status and a non-professional occupational status, was also associated with all lens changes (OR = 1.42). A \( \chi^2 \) test for trend of the association with high, medium and low SES was significantly \( (P = 0.01) \) related to an increased risk of lens changes. In analyses limited to those with nuclear only or cortical only opacities, lower SES was also positively associated with both nuclear (OR = 1.91) and cortical (OR = 1.42) opacities.

Regular users of nutritional supplements were less likely to have all lens changes (OR = 0.78) and cortical opacities (OR = 0.77). Given the apparent differences...
in supplement use by age, subgroup analyses were conducted among participants <70 years and ≥70 years. Among the subgroup of participants <70 years, associations with nutritional supplements remained significant \((P < 0.05)\) for all lens changes \((OR = 0.72)\) and cortical opacities \((OR = 0.71)\). Among older participants, no associations were found.

To explore these results further, we separately evaluated associations with multivitamins or with cod liver oil in each of these age groups. In both age groups, use of multivitamins was less frequent than use of cod liver oil. However, among those <70 years, the OR for use of multivitamin supplements were lower than for use of cod liver oil and \(P\)-values were <0.1. For multivitamins,
OR were 0.74 (95% CI: 0.52–1.06) for all lens changes and 0.70 (95% CI: 0.47–1.05) for cortical only opacities; for cod liver oil, OR were 0.89 (95% CI: 0.65–0.22) for all lens changes and 0.88 (95% CI: 0.40–0.93) for cortical only opacities (Table 5). Among those ≥70 years, no regular multivitamin users (as defined) were found in the group without opacities (n = 95). Results of analyses, based on age-sex adjusted logit estimates, showed non-significant OR higher than one for both types of supplement use.

For evaluations of risk factors for specific cataract types, an approach based on single type of opacities is preferable, such as the one we used here. For completeness, we also examined associations with any type of lens opacities, i.e. the presence, in at least one eye, of any gradable PSC (n = 162), nuclear (n = 803) or cortical (n = 1404) lens opacities, regardless of the presence of co-existing opacities. Results suggest that the use of nutritional supplements was related to a decreased risk of any PSC (OR = 0.56, 95% CI: 0.31–1.02) and any cortical (OR = 0.80, 95% CI: 0.64–1.00) opacities, but not to any nuclear opacities (OR = 0.90, 95% CI: 0.65–1.26). For any cortical opacities, odds ratios remained significantly low at ages <70 years (OR = 0.75,
95% CI : 0.59–0.96) and were over one and not significant at ages ≥70.

The relationship between supplement use and lens status was also evaluated in subgroups according to their visual acuity. Among those with visual acuity worse than 20/40 (n = 515), OR were over unity, but not statistically significant (data not shown). These results suggest that individuals began using supplements because of their visual symptoms, such as decreased visual acuity. In contrast, among those with visual acuity 20/40 or better (n = 3700), OR were under unity and suggested somewhat stronger, decreased risks. The results showed OR = 0.74 (95% CI : 0.59–0.92) for all lens changes, and 0.74 (95% CI : 0.58–0.92) for cortical only opacities.

DISCUSSION

Using a standardized and reproducible system (LOCS II) to classify lens opacities, the large sample size of the BES allowed detailed analyses of cataract prevalence and risk factors in a black population. Results support an association between demographic characteristics and lens changes, including nuclear and cortical opacities. In addition, the BES is the first study we know that suggested a relationship between regular intake of any nutritional supplements and a decrease in lens opacities in a black population. These results thus require confirmation. After controlling for demographic and other variables, regular users of nutritional supplements had a one-fourth lower risk of lens changes, and specifically, of cortical only opacities, than non-users. These findings are similar to the results of studies in white populations.6,11,12,14,15 The decreased risks were found mainly at ages <70 years and in regular users of multivitamin supplements, but not at older ages. A discussion of these issues follows.

Demographic Factors

Age, as expected, was associated with all lens changes and with single nuclear and cortical opacities. For every increase of 10 years, the age effect on risk was almost double for nuclear (OR = 6.8) than for cortical (OR = 3.6) opacities. Our results also confirmed the association of all lens changes, nuclear and cortical opacities with lower SES, an index combining educational and occupational status. Data from studies of various designs and diverse populations have consistently documented similar associations in all cataract types.3–6,8 The association could be related to environmental influences on cataractogenesis through lifestyle or health-related behaviours, such as diet, smoking, sunlight exposure, or use of health services, or to general health status.

Women were almost one and a half times more likely to have lens changes and cortical opacities than men (Table 4). A gender difference in cortical opacities is a consistent finding across studies. The first National Health and Nutrition Examination Survey (NHANES I),6 the Lens-Opacities Case-Control Study,6 and a case-control study in Italy8 also reported that women are at increased risk of cortical opacities. The population-based study in Beaver Dam13 also reported a higher prevalence of cortical opacities in women than in men of the same age. In the BES, the association of female gender and all lens changes is probably due to the parallel association of female gender and cortical opacities, which were the most frequent type of lens change. In the Framingham Eye Study,3 all senile lens changes were also more prevalent in women than men.

Nutritional Factors

According to the second US Health and Nutrition Examination Survey (NHANES II), almost 35% of the US adults take vitamin/mineral supplements at least once a week, with 36% of the white and 27% of the black population reporting such use.19 Therefore, the frequency of nutritional supplement use in Afro-Americans is similar to that of BES Afro-Caribbeans (Table 2). To obtain a rigorous definition, only those who reported a regular intake at least a year prior to the study visit were considered as supplement users.6 Regardless of the length of supplement use, people with opacities reported a less frequent intake than those with no opacities (Table 2). However, the apparent protective effect on lens opacities was not stronger in long-term supplement users, i.e. ≥2 years or ≥5 years, (data not shown). Few participants reported taking supplements of individual micronutrients, so that associations with specific nutritional supplements could not be evaluated with adequate statistical power. However, a less frequent intake of each specific supplement (except vitamin K) was reported in people with opacities than without opacities (Table 2).

Reporting inaccuracies undoubtedly occurred, but they are unlikely to differ markedly between study groups. Such random misclassification would affect the ability to detect associations, but would not necessarily cause biases. The differences between groups also persisted after multivariate adjustment for confounding variables (Table 4); they were not statistically significant for the nuclear group, which could be due to the smaller size of this group. Furthermore, consistent results were found when evaluating associations with opacities using different definitions, that is, single types (cortical only, nuclear only) or any types (any cortical, any nuclear).
The possibility of confounding was explored by examining the patterns of supplement use in various subgroups. The differences in supplement intake between those with no opacities and people with all lens changes or cortical only opacities were consistent across ages 40–69 years, gender, education and occupation subgroups (Table 3), and persisted in multivariate analyses (Table 4).

The association was seen in the overall study population and in subanalyses based on those aged 70 years (n = 3308), but not on the older age group (n = 995), where the opposite trend was suggested, although no significant age interaction effect was found. Given the prevalence study design, it was not possible to obtain accurate histories of supplement intake prior to cataract development. The likelihood of using nutritional supplements after cataract diagnosis or loss of visual acuity could be higher in the older than in the younger age group, which may offer an explanation for the findings. Given the prevalence study design, it was not possible to obtain accurate histories of supplement intake prior to cataract development. The likelihood of using nutritional supplements after cataract diagnosis or loss of visual acuity could be higher in the older than in the younger age group, which may offer an explanation for the findings. Alternatively, older individuals with cataract may be more susceptible to recall bias, which could partly explain their higher reporting of supplement use, as compared to those with no opacities (Table 3). It is also possible that older people with opacities use more supplements than those without opacities due to real or perceived differences in general health status between these groups.

In the US, self-reported reasons for using nutritional supplements include: (a) to compensate for perceived dietary deficiencies, (b) to improve the sense of health and well-being, or c) to promote longevity.\textsuperscript{20,26} It is very likely that the BES population used nutritional supplements for similar reasons, especially given media advertising that promotes the use of nutritional supplements. Thus, nutritional supplement use may be simply a marker of health awareness, which leads to an improved health status and possibly to a decreased cataract risk. To explore this issue, we examined the interrelationships among use of supplements, lens status and use of routine (nonproblem related) medical or eye care in the previous year by age. The results, shown in Table 6, confirmed that people having routine medical or eye examinations, a probable indicator of health consciousness, were more likely to be supplement users. At ages <70 years, however, people with lens changes or cortical only opacities consistently used fewer nutritional supplements than persons without opacities, regardless of routine health examinations. These indicators of health care behaviour, therefore, do not seem to explain the association between cataract and supplement usage.

The results of the BES and the magnitude of the OR resulting from the analyses of nutritional supplements are similar to those found in other studies conducted in predominantly white populations. What is the rationale for these findings? Oxidation of lens proteins appears to play a role in cataract aetiology.\textsuperscript{27,28} Therefore, several studies have explored associations of lens opacities to antioxidant nutrient status, including use of supplements, with generally similar results. In the Lens Opacities Case-Control Study\textsuperscript{6} regular use of multivitamin supplements

<table>
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<tr>
<th>Factors</th>
<th>No opacities</th>
<th>All lens changes</th>
<th>Nuclear only</th>
<th>Cortical only</th>
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<td>12.7</td>
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<td>15.9</td>
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</table>

* n <10.
*a At least once a week for at least one month, which began at least a year prior to the study interview.
for at least a year decreased risk for all cataract types. Low risks were found in people with a higher dietary intake of individual vitamins with antioxidant potential, including vitamin C, E, and carotene and riboflavin; biochemical data from this study showed associations with riboflavin status and plasma vitamin E.\textsuperscript{6,7} In the Physicians’ Health Study,\textsuperscript{14} men who used multivitamin supplements tended to experience a decreased risk of cataract. Associations of a decreased cataract risk and individual nutritional supplements, such as vitamin C,\textsuperscript{11,12} and vitamin E\textsuperscript{11} were also reported in other studies. The role of antioxidants is supported by studies using biochemical markers, which report associations of cataract with an antioxidant index, which included plasma levels of vitamin C, vitamin E and carotenoids;\textsuperscript{16} and with plasma antioxidants, such as vitamin E.\textsuperscript{7,17,18} Supportive evidence for a possible protective effect of nutritional supplements on cataract risk was found in two clinical trials in China,\textsuperscript{13} where the use of multivitamins and mineral supplements was associated with increased prevalence of nuclear opacities. These results suggest that the antioxidant properties of some supplements, e.g. vitamins C or E alone or in multivitamins, could explain the associations with a decreased cataract risk, but there may be other components of multivitamins that offer protection.\textsuperscript{14} Most multivitamins contain relatively small amounts of antioxidants and include several other vitamins and minerals.

While the findings from the BES support a protective effect of nutritional supplements on risk of opacities, especially at ages <70 years, they raise some interesting questions on the underlying pathways for the association. Data from NHANES\textsuperscript{29} showed that multivitamins were the most frequent supplements used daily (16%) in the US, while daily intake of vitamin A, including cod liver oil, was very infrequent (1.2%). In the BES, however, cod liver oil was the most commonly used supplement, along with multivitamins (Table 2). Among participants <70 years, results from the evaluation of an independent effect of these supplements suggested that multivitamin supplements were more likely to contribute to a protective effect than cod liver oil. However, the possible protective effect of cod liver oil cannot be ruled out. Therefore, although the decreased risk of lens opacities in supplement users could be related to the antioxidants in multivitamins, additional explanations are possible. Cod liver oil could play a role through the antioxidant mechanism, as it provides a source of vitamin A (e.g. 600 IU per capsule in the most popular brand of cod liver oil in Barbados). However, since cod liver oil provides mainly the preformed vitamin A, rather than the carotenoid sources of vitamin A, its antioxidant actions may be limited.\textsuperscript{30} Furthermore, cod liver oil is rich in omega-3 polyunsaturated fatty acids, which may increase susceptibility to oxidative damage by free radical generation.\textsuperscript{31} The plausible link between antioxidant potential and decreased risk of cataract from such supplementation is unclear. Alternative mechanisms provided by this supplement should be considered.

Although our analyses controlled for a number of relevant variables, it is possible that the results are due to unadjusted confounding. Additional information to clarify our findings will result from the follow-up of the BES cohort in the ongoing Barbados Incidence Study of Eye Diseases. These results offer the potential for an intervention for cataract reduction at ages <70 years, which needs to be confirmed in controlled clinical trials.

Furthermore, we have previously reported a higher prevalence of cortical opacities in the black versus the white population of the BES.\textsuperscript{24} Comparisons with other studies in whites also suggest that populations of African origin are more frequently affected by cortical cataract. Given the high prevalence of lens opacities, any decrease in cataract risk may have important public health implications.

CONCLUSIONS
All lens changes in the black BES population, including nuclear only and cortical only opacities, were positively related to indicators of low SES and suggest environmental influences on cataractogenesis. Similar findings have been reported in white and Asian populations, thus offering a possibility for modification of cataract risk. Regular users of nutritional supplements were less likely to have lens changes and cortical opacities than non-users or occasional users. The effect was mainly present at ages <70 years, and was not explained by any of the confounding variables examined. The BES results are consistent with other evidence indicating a decreased risk of cataract in supplement users. This evidence is being evaluated in ongoing clinical trials.

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