Racial Differences in Lens Opacity Incidence and Progression: The Salisbury Eye Evaluation (SEE) Study

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Purpose. To evaluate racial differences in nuclear and cortical lens opacity incidence and progression over a 2-year period in an older American population.

Methods. Prospective population-based cohort study of a multiethnic population of 2520 people (26% African-American and 74% Caucasian), 65 to 84 years of age, living in Salisbury, Maryland. Data at baseline included race, education level, past steroid use, smoking status, alcohol status, sunlight exposure, and history of hypertension and diabetes. Lens photographs were taken at baseline and at 2-year follow-up and were graded using the Wilmer grading scheme. Multiple logistic regression models were used to examine the independent associations between race, as well as other risk factors, and incidence and progression of cortical and nuclear opacities.

Results. African-Americans had lower rates of nuclear opacity incidence (Odds Ratio [OR]: 0.52; 95% Confidence Interval [CI]: 0.35–0.76) and nuclear opacity progression (OR: 0.60; 95% CI: 0.38–0.92) compared with Caucasians. African-Americans had higher rates of cortical opacity incidence (OR: 1.90; 95% CI: 1.21–2.98) and cortical opacity progression (OR: 1.72; 95% CI: 1.21–2.45) compared with Caucasians. Additionally, nuclear opacity incidence was associated with age, female sex, and current smoking status. Nuclear progression was associated with past smoking and current smoking. Cortical opacity incidence was associated with female sex, Ultraviolet-B exposure, and a history of diabetes. Cortical opacity progression was associated with current smoking status.

Conclusions. Differences by race in the type of cataract incidence and progression, even adjusting for personal and environmental risk factors, deserve further exploration.

Keywords: cataract, lens opacity, population-based study, longitudinal study, African-American, Caucasian

Cataracts are the leading cause of low vision both globally[1] and within the United States.[2] Understanding the epidemiology of cataract, including incidence and progression of various subtypes, furthers the understanding of associated risk factors and the plans for future health care needs. A number of population-based longitudinal studies in recent years have characterized lens opacities across various ethnicities. For example, lens opacity development in persons of European descent has been evaluated in the Framingham Eye Study,[3] the Italian-American Cataract Study Group,[4] the Beaver Dam Study,[5] the Priverno Eye Study,[6] the Melbourne Visual Impairment Project,[7] and the Blue Mountain Eye Study.[8] Persons of African descent were evaluated in the Barbados Eye Study[9] and Latinos were studied in the Los Angeles Latino Eye Study.[10] The different grading systems, definitions of incidence and progression, and intergrader variation across the studies make comparisons of incidence and progression between ethnicities difficult. One author pointed out that by using varying definitions of cataracts, a 3-fold difference in cataract incidence was observed within their own study.[7] However, no single study to date has had a sufficiently large and diverse population to comprehensively evaluate ethnic differences in lens opacity incidence and progression.

The purpose of this study was to assess differences in lens opacity progression and incidence rates between older African-Americans and Caucasians enrolled in the Salisbury Eye Evaluation Project over a 2-year period.

Methods

The Salisbury Eye Evaluation (SEE) project is a population-based longitudinal study of the impact of visual impairment and age-related eye diseases in older adults.[11] The project identified a random sample of people, 65 to 84 years of age, living in Salisbury, Maryland in 1993–1995 and, in all, 2520 (65%) participated in a home interview and an eye examination at the SEE clinics. Additional population details and recruitment methods have been previously described.[11] Institutional Review Board approval was obtained from the Joint Committee on Clinical Investigation of the Johns Hopkins School of Medicine, and participants gave written informed consent.

Participants filled in questionnaires on exposure to sunlight and smoking and alcohol use. Ultraviolet-B (UV-B) exposure for each individual was calculated based on a previously described empirical model integrating an individual's ocular-ambient exposure, fraction of time spent outdoors, and the protective effect of hats and eyewear.[12] Medication use was based on observed medications provided by participants. A medical history questionnaire was administered and blood taken for analyses of glycosylated hemoglobin. At the examination site,

height and weight were measured using a standard protocol.[13] Lens photographs of participants were taken after pupil dilation. Two nuclear photographs of each eye were taken using a photo slit lamp (Topcon SL-5D; Topcon Corporation, Tokyo, Japan), with the slit beam set at a height of 9 mm and a width of 0.1 mm, and angled at 40°. Cortical photographs were taken with a retro-illumination camera (Neiz Instrument Company, Tokyo, Japan), focused just posterior to the pupillary margin.

The Wilmer Eye Institute Photography Service processed all photos using standard techniques. Photographs for each eye were placed in separate plastic sheets and were graded independently of knowledge of the status of the opposing eye. Photographs were graded for type and severity of opacity using the Wilmer grading scheme. For photographs at baseline and 2 years postbaseline, two graders independently assessed images of each eye and the grading was done without knowledge of the status of the fellow eye or of prior photograph grades. Nuclear opacity was graded on a four-point decimalized scale by comparing the photo with a series of four photographic standards.[14] Cortical opacity was graded by estimating how much area in 1/16ths was covered by the opacity.[15] For photos at baseline and 2 years postbaseline, if the two graders disagreed by more than 0.3 units for nuclear or 1/16 unit for cortical, the photos were regraded by a third grader (SW) and open adjudication was done. Eyes with cataract surgery prior to baseline were excluded from the analysis.

To ensure high intra- and intergrader reliability, the graders evaluated a panel of 53 photographs initially and at various time points during the 2-year study. The interobserver agreement at baseline was 0.92 for the nuclear photographs and 0.95 for the cortical photographs. The kappa (κ) value for intraobserver agreement over time was 0.83 for nuclear opacities and 0.81 for cortical opacities. There was no evidence of drift in gradings during the study.

Definitions

We defined lens opacity based on the Wilmer grading scheme with nuclear opacity as a grade of 2.0 or higher and cortical opacity as 2/16 or higher. Nuclear incidence was defined as: among eyes with nuclear grade less than 2 (eyes at risk of nuclear opacity), incident opacity was the development of a grade of 2 or more at 2 years, with a change of at least 0.3 units. Cortical incidence was defined as: among eyes with less than grade 2/16 at baseline (eyes at risk of cortical opacity), incident opacity was the development of a grade of 2/16 or higher at 2 years with an increase of at least 2/16. Nuclear progression was defined as: among eyes with baseline opacity between 2.0 and 3.7, the grade increasing by at least 0.3 units. Cortical progression was defined as: among eyes with baseline opacity of at least 2/16, the grade increasing by at least 2/16.

Race was obtained from the Medicare database. Hypertension was based on self-report of physician diagnosis or blood pressure readings taken in the clinic. Diabetes was defined as self-report of a physician diagnosis plus antidiabetic medication use or a hemoglobin A1C of 7.0% or more. Body mass index (BMI) was calculated as weight in kilograms over height in meters squared. All other variables—education level, past steroid use, smoking status, and alcohol status—were based on self-report.

Statistical Analyses

Contingency tables analysis was used to compare the characteristics of study subjects included and excluded from the analyses. For each opacity type incidence, progression and cataract surgery rates stratified by race are presented. Multiple logistic regression models were used to examine the independent associations between incidence/progression of cortical/nuclear opacities and putative risk factors. To have results comparable with previous studies, we chose to report odds ratios (ORs) and 95% confidence intervals (CIs) (as opposed to Poisson regression). The generalized estimating equation (GEE) approach was used to correct the SE values of the estimates to account for the correlation between eyes of the same subject (procedure GENMOD in SAS, binomial distribution, logit link function, exchangeable correlation structure; SAS Institute, Cary, NC).

Sensitivity analyses was performed, assessing the potential effect of cataract surgery on incidence and progression by considering rates if all eyes that underwent surgery in each subgroup had been classified as incident or progression cases.

Results

Sample Population

A total of 2520 individuals participated (65% of eligible population) and we have previously reported on the comparison of participants and those who chose not to participate, which showed no difference by race, self-reported vision status, sex, or education status once adjusted for age.[11] All participants included in the analysis had a follow-up time of 2 years.

An analysis of the population at 2 years showed that the 625 individuals excluded from the analysis due to bilateral cataract surgery at baseline ($n = 246$), loss to follow-up (including due to death) ($n = 252$), or no available images at either point of time ($n = 127$) were more likely to be older, to have a history of steroid use, and to be current smokers (Table 1). Of the population included in the analysis, African-Americans were more likely than Caucasians to have <12 years of education ($P < 0.001$), diabetes ($P < 0.001$), BMI > 30 ($P < 0.001$), a history

Table 1. Baseline Characteristics of Analysis Population Compared With Excluded Individuals

Baseline Characteristic	Included* $n = 1895$, % (n)	Excluded $n = 625$, % (n)	P Value
Age group, y			**<0.0001**
65–69	34.2 (648)	21.1 (132)	
70–74	33.9 (642)	30.7 (192)	
75–79	21.2 (402)	24.5 (153)	
80+	10.7 (203)	23.7 (148)	
Females	57.6 (1092)	58.7 (367)	0.61
African-Americans	26.9 (510)	25.0 (156)	0.33
<12 years of education	50.9 (965)	53.4 (334)	0.26
Diabetes	18.0 (341)	20.7 (129)	0.14
Body Mass Index >30	31.1 (589)	27.6 (173)	0.11
History of steroid use	8.5 (161)	12.9 (81)	**0.001**
History of high blood pressure	54.9 (1040)	57.0 (356)	0.35
Smoking status			**0.04**
Never	40.9 (775)	36.5 (228)	
Past	45.3 (858)	46.5 (291)	
Current	13.8 (262)	17.0 (106)	

Statistically significant results in bold.

* With grades of at least one type of opacity in at least one eye at both baseline and 2 years follow-up. Excluded individuals include those lost to follow-up, bilateral cataract surgery at baseline, and no image available.

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Table 2. Baseline Characteristics of Analysis Population by Race

Baseline Characteristic	African-American $n = 510$, % (n)	Caucasian $n = 1385$, % (n)	P Value
Age group, y			0.71
65–69	36.3 (185)	33.4 (463)	
70–74	32.7 (167)	34.4 (476)	
75–79	20.8 (106)	21.3 (295)	
80+	10.2 (52)	10.9 (151)	
Females	61.0 (311)	56.3 (780)	0.07
<12 years of education	74.7 (381)	42.1 (583)	**<0.001**
Diabetes	29.6 (151)	13.9 (193)	**<0.001**
Body Mass Index >30	41.3 (211)	27.4 (379)	**<0.001**
History of steroid use	5.4 (28)	9.6 (133)	**0.004**
History of high blood pressure	63.7 (325)	51.7 (716)	**<0.001**
Smoking status			**0.001**
Never	40.6 (207)	40.9 (566)	
Past	39.2 (200)	47.7 (661)	
Current	20.2 (103)	11.4 (158)	

Statistically significant results in bold.

of steroid use ($P = 0.004$), a history of high blood pressure ($P < 0.001$), and current smoking status ($P = 0.001$) (Table 2).

Pure and Mixed Opacity Incidence

By selecting eyes with nuclear grade <2.0 at baseline, cortical grade <2 at baseline and with gradable photographs at the 2-year visit, we evaluated pure and mixed opacity incidence. For Caucasians, 153/1254 (12.2%) developed pure nuclear, 32/1254 (2.9%) developed pure cortical, and 5/1254 (0.4%) developed mixed opacities. For African-Americans, 19/356 (5.3%) developed pure cortical, 13/356 (3.7%) developed pure nuclear, and 2/356 (0.6%) developed mixed opacities.

Nuclear Opacity Incidence and Progression

The 2-year incidence of nuclear opacity was lower in African-Americans (6.3%) than that in Caucasians (12.1%), with an OR of 0.52 (95% CI: 0.35–0.76) after adjusting for baseline severity level and correlation between eyes of the same subject (Table 3). In the general population, nuclear incidence was associated with a baseline grade between 1.0 and 1.9 (OR: 5.13; 95% CI: 2.91–9.06). After adjustment for multiple risk factors, the incidence was still lower among African-American ethnicity (OR 0.45; 95% CI: 0.28–0.71) (Table 4). Females had higher nuclear incidence than that of males, with rates of 8.5% vs. 3.4% in African-Americans and 13.4% vs. 10.5% in Caucasians (Table 3), with an overall OR of 1.57 (95% CI: 1.10–2.26) after controlling for other risk factors (Table 4). The incidence of nuclear opacities also increased with age (OR: 1.09; 95% CI: 1.05–1.13) and current smoking status (OR: 2.13; 95% CI: 1.25–3.66) (Table 4). We found no association of nuclear opacity incidence with education level, steroid use, ex-smoker status, alcohol use, hypertension, diabetes, or BMI > 30.

The progression rate of nuclear opacities was lower in African-Americans (22.9%) than that in Caucasians (28.7%), with an OR of 0.60 (95% CI: 0.38–0.92) after adjusting for baseline severity level and correlation between eyes of the same subject (Table 5). In the general population, baseline nuclear severity grade ≥3 was associated with lower rates of nuclear progression (OR: 0.32; 95% CI: 0.21–0.48). The racial difference in progression was not statistically significant in our multivariate analysis (Table 4). If we refined our model to include only age, race, and smoking status (parsimonious

Table 3. Nuclear Opacity Incidence* and Surgery Rates by Ethnicity, Age, and Sex

	African-Americans						Caucasians					
	Males			Females			Males			Females		
Age Group, y	Eyes at Risk	Incidence % (n)	Surgery % (n)	Eyes at Risk	Incidence % (n)	Surgery % (n)	Eyes at Risk	Incidence % (n)	Surgery % (n)	Eyes at Risk	Incidence % (n)	Surgery % (n)
65–69	130	2.3 (3)	1.5 (2)	167	6.6 (11)	3.6 (6)	315	7.9 (25)	0.0 (0)	350	10.0 (35)	0.9 (3)
70–74	94	6.4 (6)	3.2 (3)	135	8.9 (12)	3.7 (5)	270	8.9 (24)	1.9 (5)	312	13.1 (41)	1.9 (6)
75–79	63	1.6 (1)	1.6 (1)	58	10.4 (6)	0.0 (0)	102	18.6 (19)	2.9 (3)	125	19.2 (24)	0.0 (0)
≥80	9	0.0 (0)	11.1 (1)	27	14.8 (4)	0.0 (0)	35	22.9 (8)	8.6 (3)	56	23.2 (13)	12.5 (7)
Total	296	3.4 (10)	2.4 (7)	387	8.5 (33)	2.8 (11)	722	10.5 (76)	1.5 (11)	843	13.4 (113)	1.9 (16)
Overall by ethnicity	Eyes at risk 683		Incidence % (n) 6.3 (43)		Surgery % (n) 2.6 (18)		Eyes at risk 1565		Incidence % (n) 12.1 (189)		Surgery % (n) 1.7 (27)	

* Nuclear incidence: An increase of at least 0.3 units from <2.0 at baseline to ≥2.0 at 2 years.

Table 4. Multivariate Analysis of Factors Associated With Incidence and Progression of Nuclear Opacity

Characteristic	Nuclear Incidence (*n* analyzed = 2203) Odds Ratio (95% Confidence Interval)	Nuclear Progression (*n* analyzed = 774) Odds Ratio (95% Confidence Interval)
Age (per y increase)	**1.09 (1.05–1.13)**	0.97 (0.93–1.01)
Female/Male	**1.57 (1.10–2.26)**	0.82 (0.55–1.21)
African-Americans/Caucasians	**0.45 (0.28–0.71)**	0.71 (0.43–1.16)
High school or more	0.82 (0.57–1.17)	1.02 (0.68–1.54)
Past steroid use	0.71 (0.43–1.18)	1.62 (0.76–3.45)
Smoking status		
Never	1.00	1.00
Past	1.39 (0.94–2.05)	1.31 (0.84–2.05)
Current	**2.13 (1.25–3.66)**	1.57 (0.83–3.45)
Alcohol status		
Never	1.00	1.00
Past	0.83 (0.50–1.37)	0.98 (0.58–1.67)
Current	0.90 (0.59–137)	0.89 (0.53–1.51)
History of hypertension	1.26 (0.91–1.77)	0.87 (0.61–1.24)
Diabetes	0.94 (0.60–1.49)	0.78 (0.47–1.32)
Body Mass Index >30	1.21 (0.84–1.73)	1.35 (0.89–2.06)

Caucasians are used as reference group. SE values have been corrected to account for the correlation between eyes of the same subject. Statistically significant results in bold.

model), we did find an association of nuclear progression with past smoking (OR: 1.58; 95% CI: 1.08–2.30) and current smoking (OR: 2.00; 95% CI: 1.52–3.47), but racial differences were still not significant. We found no significant association of nuclear progression with sex, age, education, past steroid use, alcohol use, hypertension, diabetes, or BMI > 30.

Cortical Opacity Incidence and Progression

The incidence rate of cortical opacity was higher in African-Americans (6.9%) than that in Caucasians (3.0%), with an OR of 1.90 (95% CI: 1.21–2.98) (Table 6), after adjustment for baseline severity and correlation between eyes of the same individual. The incidence of cortical opacity was associated with a baseline grade between 1 and 1.9 (OR: 3.72; 95% CI: 2.31–5.99). Females had higher cortical incidence with rates of 7.2% vs. 6.5% in African-Americans and 3.8% vs. 2.2% in Caucasians (Table 6), for an overall OR of 1.93 (95% CI: 1.18–3.16). The racial difference persisted after adjustment for multiple factors (OR: 1.97; 95% CI: 1.17–3.32) (Table 7). Increased incidence of cortical opacity was also associated with UV-B exposure (OR: 3.72; 95% CI: 1.04–13.1) and a history of diabetes (OR: 1.80; 95% CI: 1.06–3.04) (Table 7). We found no association of cortical opacity incidence with age, education level, past steroid use, smoking status, alcohol use, hypertension, or BMI > 30.

The progression rate of cortical opacities was higher in African-Americans (38.4%) than that in Caucasians (22.8%), with an OR of 1.72 (95% CI: 1.21–2.45) (Table 8) after adjustment for baseline severity and correlation between eyes. The greater the severity at baseline, the more likely the progression (OR: 1.24 per unit of severity increase; 95% CI: 1.06–1.44). Multivariate analysis revealed that African-American ethnicity (OR: 1.85; 95% CI: 1.28–2.68) and current smoking status (OR: 1.89; 95% CI: 1.03–3.47) were significantly associated with cortical opacity progression (Table 7). UV-B exposure was also associated with progression, but the confidence interval overlapped 1.0 (Table 7). We found no association of age, sex, education level, steroid use, past smoking, alcohol use, hypertension, diabetes, or BMI > 30 on cortical opacity progression.

We allowed eyes that had gone on to surgery, where we could not measure incidence or progression, to be presumptive cases of incidence or progression in our sensitivity analyses. We found statistically significant higher rates of cortical incidence and progression in African-Americans and higher nuclear incidence in Caucasians, as we did above. Progression of nuclear opacity was higher in Caucasians but still not statistically significant.

We also evaluated factors associated with nuclear and cortical lens opacity incidence for individuals without any type of cataract at baseline. The results were essentially similar to those above.

Discussion

The Salisbury Eye Evaluation is the first longitudinal evaluation using detailed lens grading of a multiethnic population: 2520 individuals 65–84 years of age comprised of 26.4% African-Americans and 73.6% Caucasians at baseline. This study demonstrates substantial differences by opacity type in lens opacity incidence and progression rates between African-Americans and Caucasians over a 2-year period.

Prevalence data of this population at baseline showed that African-Americans were 4-fold more likely to have cortical opacities, whereas Caucasians were 2.1-fold more likely to have nuclear opacities.[16] After 2 years of follow-up, we found a similar trend with incidence and progression: African-Americans were almost twice as likely as Caucasians to have cortical opacity incidence and progression; Caucasians were almost twice as likely as African-Americans to have nuclear opacity incidence and progression. However, the racial difference in nuclear opacity progression became nonsignificant when other risk factors were considered.

Our results extend the findings of our own prevalence data and a number of studies showing higher prevalence of cortical opacities in African-Americans[16–18] and higher prevalence of nuclear opacities in Caucasians.[19–21] The Barbados Eye Study, whose sample population consisted of <3% Caucasians and was not population based (it was an extension of a case-control study), reported a significantly higher cortical incidence rate

Table 5. Nuclear Opacity Progression* and Surgery Rates by Ethnicity, Age, and Sex

	African-Americans						Caucasians					
	Males			Females			Males			Females		
Age Group, y	Eyes at Risk	Incidence % (*n*)	Surgery % (*n*)	Eyes at Risk	Incidence % (*n*)	Surgery % (*n*)	Eyes at Risk	Incidence % (*n*)	Surgery % (*n*)	Eyes at Risk	Incidence % (*n*)	Surgery % (*n*)
65–69	10	30.0 (3)	0.0 (0)	24	20.8 (5)	0.0 (0)	54	44.4 (24)	5.6 (3)	91	30.8 (28)	6.6 (6)
70–74	21	23.8 (5)	9.5 (2)	31	19.4 (6)	6.5 (2)	84	30.1 (26)	5.9 (5)	119	26.9 (32)	5.9 (7)
75–79	20	10.0 (2)	5.0 (1)	40	30.0 (12)	0.0 (0)	76	34.2 (26)	10.5 (8)	89	24.7 (22)	9.0 (8)
≥80	10	20.0 (2)	20.0 (2)	19	26.3 (5)	10.5 (2)	38	15.8 (6)	7.9 (3)	48	16.7 (8)	12.5 (6)
Total	61	19.7 (12)	8.2 (5)	114	24.6 (28)	3.5 (4)	252	32.5 (82)	7.4 (19)	347	25.9 (90)	7.8 (27)
Overall by ethnicity	Eyes at risk 175		Progression % (*n*) 22.9 (40)		Surgery % (*n*) 5.1 (9)		Eyes at risk 599		Progression % (*n*) 28.7 (172)		Surgery % (*n*) 7.7 (46)	

* Nuclear progression: An increase of at least 0.3 units in eyes between 2.0 and 3.7 at baseline.

Note: In all, 87 eyes with baseline nuclear grade >3.7 not included on the table had surgery between visit 1 and visit 2; 291 eyes with baseline nuclear grade >3.7 and grades available in round 2 not included.

Table 6. Cortical Opacity Incidence* and Surgery Rates by Ethnicity, Age, and Sex

	African-Americans						Caucasians					
	Males			Females			Males			Females		
Age Group, y	Eyes at Risk	Incidence % (*n*)	Surgery % (*n*)	Eyes at Risk	Incidence % (*n*)	Surgery % (*n*)	Eyes at Risk	Incidence % (*n*)	Surgery % (*n*)	Eyes at Risk	Incidence % (*n*)	Surgery % (*n*)
65–69	100	5.0 (5)	0.0 (0)	127	7.1 (9)	1.6 (2)	364	1.4 (5)	2.5 (9)	420	4.0 (17)	3.3 (14)
70–74	64	7.8 (5)	6.3 (4)	85	10.6 (9)	2.4 (2)	351	2.3 (8)	3.7 (13)	405	3.7 (15)	4.0 (16)
75–79	45	8.9 (4)	4.4 (2)	46	2.2 (1)	2.2 (1)	183	2.7 (5)	7.1 (13)	212	2.8 (6)	7.1 (15)
≥80	7	0.0 (0)	28.6 (2)	21	4.8 (1)	4.8 (1)	67	4.5 (3)	4.5 (3)	105	4.8 (5)	19.0 (20)
Total	216	6.5 (14)	3.7 (8)	279	7.2 (20)	2.2 (6)	965	2.2 (21)	3.9 (38)	1142	3.8 (43)	5.7 (65)
Overall by ethnicity	Eyes at risk 495		Incidence % (*n*) 6.9 (34)		Surgery % (*n*) 2.8 (14)		Eyes at risk 2107		Incidence % (*n*) 3.0 (64)		Surgery % (*n*) 4.9 (103)	

* Cortical incidence: An increase of at least 2/16 units from <2 at baseline to ≥2 at 2 years.

Table 7. Multivariate Analysis of Factors Associated With Cortical Opacity Incidence and Progression

Characteristic	Cortical Incidence (*n* analyzed = 2485) Odds Ratio (95% Confidence Interval)	Cortical Progression (*n* analyzed = 859) Odds Ratio (95% Confidence Interval)
Age (per year increase)	1.03 (0.97–1.08)	1.00 (0.96–1.04)
Female/Male	**1.93 (1.18–3.16)**	1.40 (0.88–2.22)
African-Americans/Caucasians	**1.97 (1.17–3.32)**	**1.85 (1.28–2.68)**
High school or more	0.86 (0.53–1.40)	1.12 (0.76–1.66)
Past steroid use	1.43 (0.57–3.50)	0.70 (0.36–1.35)
Smoking status		
Never	1.00	1.00
Past	1.08 (0.63–1.85)	1.38 (0.90–2.12)
Current	1.11 (0.55–2.23)	**1.89 (1.03–3.47)**
Alcohol status		
Never	1.00	1.00
Past	1.45 (0.74–2.86)	0.61 (0.37–1.00)
Current	1.33 (0.70–2.49)	0.63 (0.39–1.01)
History of hypertension	0.84 (0.53–1.34)	0.74 (0.50–1.10)
Diabetes	**1.80 (1.06–3.04)**	0.90 (0.59–1.38)
Body Mass Index >30	0.90 (0.53–1.51)	1.08 (0.72–1.62)
Average annual Ultraviolet-B exposure (1/10 Maryland sun year)	**3.72 (1.04–13.1)**	2.33 (0.78–6.97)

Caucasians are used as reference group. SE values have been corrected to account for the correlation between eyes of the same subject. Statistically significant results in bold.

among individuals of African descent than among Caucasians, which is consistent with our results.[9]

We suspected that the racial differences in incidence rates would mirror the prevalence rates, but we hypothesized that the progression rates would be similar. That is, once a person had a lens opacity, the progression rates would not differ by race, but this was not the case. This is unlikely due to differential cataract surgery rates, which did exist with African-Americans having lower rates, but we found that progression rates of cortical cataract were greater in African-Americans and progression rates of nuclear cataract were greater in Caucasians. Moreover, our sensitivity analyses, where we allowed the surgery eyes to have progressed or become incident cases, did not change our findings.

Although our rates of lens opacity incidence and progression in the Caucasian population were within the range of previous studies, some of our results in the African-American population differed significantly from the Barbados Eye Study, the only prior longitudinal study in individuals of African descent. The Barbados Eye Study found a nuclear progression rate of 3.6% over 4 years, whereas we found a rate of 22.9% over 2 years.[9] The Barbados Eye Study also found cortical incidence rates of 22.2% and cortical progression rates of 12.5% compared with our results of 6.9% and 38.4%, respectively.[9] These differences may be due to the different age ranges of the two studies, because SEE participants were older, and also due to the different grading systems used by the two studies—the LOCS II and the Wilmer Grading Scale—which have different definitions of incidence and progression.

Previous studies of Caucasian populations have also shown a wide range of results. For example, the 5-year cortical incidence rates for Caucasians ranged from 8.0% in the Beaver Dam Eye Study,[5] which would be closer to our rate, to 28.2% in the Italian-American Cataract Study Group.[4] Nuclear incidence rates range from 11.5% in the Italian-American Cataract Study Group[4] to as high as 45.3% in the Melbourne Visual Impairment Project.[7] These differences in opacity incidence rates just within Caucasians highlight the difficulty of comparing African-American rates in one study to Caucasian rates in another and the need for a single multiethnic study to make definitive comparisons. Some of the variation between studies is due to alternate definitions of incidence and progression based on different grading scales, including the Wilmer protocol, the Lens Opacities Classification System (LOCS) II and LOCS III, and Beaver Dam Eye study grading schemes. Previous studies have also not been consistent with regard to person-level or eye-level reporting, which has increased interstudy variation; right eye,[5] at least one eye,[7,9,10] and at least one eye with vision loss to at least 20/30[4] definitions have all been utilized. We chose to report eye-level rates because we feel it is the most robust approach.

Differential use of cataract surgery has the potential to mask real differences of opacity incidence or progression between subgroups, especially if factors other than progression (such as access to care or perceived need of services) drive cataract surgery rates. No previous longitudinal studies of lens opacity have adjusted or evaluated incidence or progression rates to account for cataract surgery, even when rates were found to be as high as 17.8%.[8] We assessed the potential effect of cataract surgery by considering incidence and progression rates if all eyes that underwent surgery in each subgroup had been considered incident or progression cases. This sensitivity analysis reaffirmed our original findings of statistically significant higher rates of cortical incidence and progression in African-Americans and higher nuclear incidence in Caucasians.

The question of why there are racial differences in lens opacity incidence and progression is unclear. It is possible that we are not controlling for other, nongenetic, risk factors that affect the races differentially. It is unlikely that the ethnic differences found are due to environmental exposures of smoking or UV-B exposure as these have been considered. There may, however, be residual environmental exposures that have not been measured. Some previous studies have found associations between diet,[22] particularly lutein and zeaxanthin,[23] and cataract formation as well as racial differences in serum lutein and zeaxanthin levels,[24] which we have not considered in this study. However, the differences in incidence rates between ethnicities found in our study are larger than

TABLE 8. Cortical Opacity Progression* and Surgery Rates by Ethnicity, Age, and Sex

	African-Americans						Caucasians					
	Males			Females			Males			Females		
Age Group, y	Eyes at Risk	Incidence % (*n*)	Surgery % (*n*)	Eyes at Risk	Incidence % (*n*)	Surgery % (*n*)	Eyes at Risk	Incidence % (*n*)	Surgery % (*n*)	Eyes at Risk	Incidence % (*n*)	Surgery % (*n*)
65–69	39	43.6 (17)	5.1 (2)	71	33.8 (24)	9.9 (7)	38	13.2 (5)	7.9 (3)	47	38.3 (18)	6.4 (3)
70–74	51	27.5 (14)	3.9 (2)	101	37.6 (38)	5.9 (6)	47	25.5 (12)	6.4 (3)	80	27.5 (22)	10.0 (8)
75–79	45	46.7 (21)	2.2 (1)	61	42.6 (26)	0.0 (0)	49	14.3 (7)	14.3 (7)	87	20.7 (18)	12.6 (11)
≥80	15	33.3 (5)	13.3 (2)	42	42.9 (18)	4.8 (2)	24	20.8 (5)	16.7 (4)	62	19.4 (12)	16.1 (10)
Total	150	38.0 (57)	4.7 (7)	275	38.6 (106)	5.5 (15)	158	18.3 (29)	10.8 (17)	276	25.4 (70)	11.6 (32)
Overall by ethnicity	Eyes at risk 425		Progression % (*n*) 38.4 (163)		Surgery % (*n*) 5.2 (22)		Eyes at risk 434		Progression % (*n*) 22.8 (99)		Surgery % (*n*) 11.3 (49)	

* Cortical progression: An increase of at least 2/16 units in eyes between 2 and 14 at baseline.

those found in previous studies of lutein and zeaxanthin, making this an unlikely differential environmental exposure causing our results.[23] Given the mounting evidence for a role of genetics in opacity development, it is also possible that the racial differences we found in this study may point to genetic variation between African-Americans and Caucasians. Some complex diseases have shown large heterogeneity of genetic effect between races.[25] The Twin Eye Study, an entirely Caucasian population, showed that genetics may account for 48% of variability of nuclear opacity, whereas age and environmental factors account for 38% and 14%, respectively.[26] The Twin Eye Study also showed that genetics may explain 58% of variability in cortical opacity, whereas age and environmental factors may explain 16% and 26%, respectively.[27] The expression of several genes, including alpha,[28–33] beta,[34,35] and gamma-crystallin genes,[36,37] has been implicated in lens opacity formation. Recent studies have hypothesized that alpha crystalline proteins in particular act via molecular chaperones in the lens to protect from oxidative stress that would otherwise lead to opacity formation.[30–33] However, we know of no study that has investigated differences in genetic effects between ethnicities for cataract formation.

Interestingly, we found that age was significantly associated with only nuclear opacity incidence, not cortical opacity incidence. All previous longitudinal studies of lens opacities have found that age is strongly associated with both nuclear and cortical opacity incidence.[5–7,9,10,38] In our study, the association was in the correct direction (increased incidence with age) but was not statistically significant, which may reflect the low rate of cortical incidence in Caucasians and the wide confidence intervals.

Our results also showed that females were more likely to have nuclear and cortical opacity incidence—but not progression—as compared with males, with a ratio of approximately five females for every three males for nuclear incidence and two females for every one male for cortical incidence. Previous data have shown mixed results when evaluating sex differences with studies showing: (1) higher cortical incidence, nuclear incidence, and nuclear progression among females[9]; (2) higher nuclear incidence only among females[5]; and (3) no sex differences.[7,38]

Several previous studies of lens opacity prevalence appear to have shown that females had higher prevalence of lens opacities compared with that of males, particularly after 65 years of age,[19,21,39] which led to the hypothesis that estrogen exposure could affect lens opacification. Population-based longitudinal studies, including the Salisbury Eye Evaluation, have shown no relationship between hormone replacement therapy and lens opacity incidence or progression.[40,41]

Smoking status was also associated with nuclear opacity incidence and progression, which is consistent with a number of previous studies.[42–44] We found that current smokers were twice as likely as nonsmokers to have incidence and progression of nuclear cataracts. Past smoking was also related to nuclear opacity incidence, although the relationship was not statistically significant. Smoking was not related to incidence of cortical opacity but we did find a relationship with progression of cortical opacities, which was unexpected.

We have consistently found that UV-B light exposure is associated with cortical opacity prevalence using this population.[12] We have now found UV-B light to be related to incidence of cortical opacity as well, which is in agreement with previous studies.[45,46] Additionally, UV-B exposure was related to cortical cataract progression, although the association was not statistically significant. The association may have been stronger if we had a measure of UV-B exposure in the interim 2 years as well, because it is more likely that concurrent exposure is the more relevant variable. We have

previously reported that nuclear opacities are not associated with UV-B exposure in this population.[12]

We found that a history of diabetes is significantly associated with cortical opacity incidence, which is consistent with previous studies.[47–52] However, in contrast to some studies, we did not find an association between a history of diabetes and nuclear opacity incidence[48,53] or cortical opacity progression,[49] which may reflect the fact that progression is related to duration of diabetes and degree of control and we did not measure these variables.

In addition to the risk factors discussed above, we found that baseline opacity grade was correlated with opacity incidence and progression. The association with incidence is in part a reflection of the definitions, where the closer a baseline grade is to the cutoff of 2/16 for cortical opacities and 2.0 for nuclear opacities, the more likely the opacity will progress beyond this line over a 2-year period. However, for progression, there is some evidence that rates increase with the severity of the opacity at baseline and we found that to be the case with progression of cortical opacity; cortical severity (per unit increase in baseline severity) increased the risk of progression (OR = 1.24; 95% CI: 1.06–1.44). We did not observe that trend with nuclear opacity, which may reflect the fact that cataract surgery was more likely to intervene and we could not measure progression in the higher grades.

The greatest strength of the Salisbury Eye Evaluation is that it consists of a large, population-based multiethnic sample followed over time using identical methods for detection and monitoring lens opacities. Other strengths include the sampling strategy, use of a validated grading scheme, and high intergrader reliability. A limitation of this study is the refusal rate and loss of images leading to loss of follow-up. However, the loss was not differential with regard to race, so we do not believe it biased our conclusions regarding incidence and prevalence by race. Finally, previous longitudinal studies have had durations of 4 to 10 years, making this study of a 2-year time frame relatively short in comparison. However, longer time intervals increase the likelihood that cataract surgery will interrupt an assessment of natural incidence and progression. Other limitations include the small number of people in the incidence analysis, which results in large SE values, and the reliance on self-report for some risk factors such as smoking and alcohol use. If errors in self-reporting differ by race, bias may be introduced.

In conclusion, our study provides strong evidence for ethnic differences in lens opacity development and progression: African-Americans have higher rates of cortical incidence and progression, whereas Caucasians have higher rates of nuclear incidence and progression, although this nuclear progression difference becomes nonsignificant when other risk factors are controlled. Given that genetics have been shown to be the largest determinant of cataract variability, it is possible that the observed differences in this study may be due to differential genetic effects between races. Differences in opacity incidence and progression rates between ethnicities have the potential to create differential demand for cataract surgery. Ethnic differences in opacity development should be considered when planning for future surgical need and when evaluating potential health care disparities in the form of different cataract surgery rates.

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