Incidence of Age-Related Cataract over a 15-Year Interval

The Beaver Dam Eye Study

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Objective: To describe the long-term incidence of nuclear cataract, cortical cataract, and posterior subcapsular cataract (PSC) and to evaluate age and cohort effects on these rates.

Design: Population-based study.

Participants: Members of the Beaver Dam Eye Study cohort.

Methods: Subjects were seen in study offices for examinations (slit lamp, checking for occludable angles, dilation of pupils, lens photographs, measurement of blood pressures, and study interview).

Main Outcome Measures: Lens photographs were taken with specially modified cameras that have been maintained over the course of all study examinations. Photographs were graded according to standard protocols that have been continued throughout all the examinations.

Results: Cumulative incidence of nuclear cataract was 29.7% (95% confidence interval [CI], 28.0–31.4); cortical cataract, 22.9% (95% CI, 21.3–24.5); PSC, 8.4% (95% CI, 7.4–9.4); and cataract surgery, 17.7% (95% CI, 16.4–19.0). The cumulative incidence increased with age and was greater for women after accounting for competing events. The relationship between age and incidence of cataracts was quadratic for nuclear cataract, cubic for cortical cataract, and linear for PSC. For persons with similar ages at time of examination, those in more recent birth cohorts were less likely to have any type of prevalent cataract; the effect was significant for nuclear cataract and for cataract surgery, and the effect persisted after controlling for relevant confounders. There were apparent cohort effects on cataract incidence.

Conclusions: Age-adjusted incidence of all cataract types increased with increasing age, although the age effect was not linear for all 3 types. More recent birth cohorts are relatively protected relative to persons born earlier. Further follow-up is needed to verify the trends we report here and to determine whether cohort effects on 10-year incidence are significant. *Ophthalmology 2008;115:477–482 © 2008 by the American Academy of Ophthalmology.*

The presence and short-term incidence of age-related cataract have been widely reported[1–10]; however, less is known about the long-term incidence. Because cataract is usually slow to develop, longer follow-up is necessary to identify antecedent risk factors. Cataracts or early lens opacities are not rare in middle age,[10–15] but the effect of age on the development and progression of cataract is not well defined. Although age is the most important risk factor for cataracts, there may be cohort and period influences on cataract and cataract surgery prevalence. Understanding these patterns is likely to be important when evaluating the need for and availability of health care. The Beaver Dam Eye Study, a long-term population-based study, is uniquely designed for such evaluations. Here, we present our findings on age and cohort influences on the long-term incidence of the 3 most common forms of age-related cataract (i.e., nuclear, cortical, and posterior subcapsular) in this well-described population.

Materials and Methods

Population

Methods used to identify the population and descriptions of the population have appeared in previous reports.[16,17] In brief, a private census of the population of Beaver Dam, Wisconsin was performed from September 15, 1987 to May 4, 1988. Eligibility requirements for study participation included living in the city or township of Beaver Dam and being 43 to 84 years old at the time of the census. There were 5925 eligible individuals, institutional-

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Table 1. 15-Year Cumulative Incidence from Baseline Examinations

Sex	Age Group (yrs)	Nuclear Cataract: N at Risk	Nuclear Cataract: Main Cumulative Incidence	Nuclear Cataract: HR	Nuclear Cataract: 95% CI	Nuclear Cataract: P Value	Cortical Cataract: N at Risk	Cortical Cataract: Main Cumulative Incidence	Cortical Cataract: HR	Cortical Cataract: 95% CI	Cortical Cataract: P Value
Women	43–54	624	15.5%				632	15.2%			
	55–64	483	42.3%	4.2	3.1–5.5	<0.001	477	32.7%	3.3	2.4–4.3	<0.001
	65–74	373	52.1%	11.3	8.3–15.4	<0.001	388	29.8%	4.2	3.0–5.8	<0.001
	75+	81	51.9%	22.8	13.5–38.4	<0.001	112	24.5%	7.1	4.2–11.9	<0.001
Total (trend)		1561	34.0%				1609	24.4%			
				3.1	2.7–3.5	<0.001			1.9	1.7–2.2	<0.001
Men	43–54	555	9.0%				553	12.4%			
	55–64	453	29.1%	4.5	3.1–6.5	<0.001	436	24.9%	2.9	2.0–4.0	<0.001
	65–74	301	46.4%	16.6	11.3–24.5	<0.001	301	33.4%	5.9	4.1–8.5	<0.001
	75+	83	37.5%	27.0	14.7–49.4	<0.001	99	21.3%	9.0	4.8–16.8	<0.001
Total (trend)		1392	24.8%				1389	21.1%			
				3.5	3.0–4.1	<0.001			2.3	1.9–2.6	<0.001
Age-adjusted Men vs Women				0.7	0.6–0.8	<0.001			0.9	0.7–1.1	0.178
Total	43–54	1179	12.4%				1185	13.9%			
	55–64	936	36.0%	4.2	3.4–5.3	<0.001	913	29.0%	3.1	2.5–3.8	<0.001
	65–74	674	49.5%	13.2	10.4–16.7	<0.001	689	31.4%	4.9	3.8–6.2	<0.001
	75+	164	44.6%	24.1	16.2–35.7	<0.001	211	23.0%	7.8	5.3–11.7	<0.001
Total (trend)		2953	29.7%				2998	22.9%			
				3.2	2.9–3.6	<0.001			2.1	1.9–2.3	<0.001

CI = confidence interval; HR = hazard ratio.

ized and noninstitutionalized; 4926 participated in the examination phase between March 1, 1988 and September 14, 1990. Ninety-nine percent of the population was white. All participants were invited for 5-year (3684 examined), 10-year (2764 examined), and 15-year (2119 examined) follow-up examinations. The primary reason for nonparticipation was death. Comparisons between participants and nonparticipants at baseline and at the 5-, 10-, and 15-year follow-up examinations have appeared in previous publications.[17–20] In general, nonparticipants were older, had higher blood pressures, and were more likely to have had cataract and age-related macular degeneration at baseline. The mean and median times between the baseline and 15-year follow-up examinations were 14.9 years (standard deviation, 0.5) and 14.8 years, respectively.

Procedures

Approval was granted by the institutional review board at the University of Wisconsin, and informed consent was obtained from each participant at the beginning of each examination. The same procedures were followed at each examination. Those eyes judged to have a low risk of angle closure had their pupils dilated pharmacologically. A photograph was taken of the lens of each eye using an SL5 Photoslit Lamp camera (Topcon, Paramus, NJ). The camera had been specially modified for this study so that uniform photographs could be obtained for each participant.[21] Retroillumination photographs of the lens were taken using a CR-T camera (Neitz, Torrance, CA). This camera was also modified specifically for this study to obtain uniform photographs.[21] Ektachrome 200 ASA film (Kodak, Rochester, NY) was used.

Slit-lamp photographs were judged for severity of nuclear sclerosis with a set of 4 standard photographs of increasingly severe nuclear sclerosis resulting in 5 levels of severity. Severity greater than standard 3 was considered to be nuclear cataract. Retroillumination photographs were used to grade cortical and posterior subcapsular opacities. A circular grid was used to define 9 areas. The grader estimated the percent of involvement in each segment, and a weighted average based on segment size was used to calculate the total area of the lens (considering the lens as a plane surface) involved with cortical and posterior subcapsular opacity, resulting in a continuous measure of severity from zero to 100. Cortical cataract was defined as involvement of more than 5% of the lens area. Posterior subcapsular cataract (PSC) was defined as 5% or more of any lens segment.[21] For incidence analyses, we refer to the dichotomies of nuclear cataract, cortical cataract, or PSC as defined above. Persons (eyes) included in incidence analyses in this article are those persons who were seen at the baseline examination, did not have the types of age-related cataracts or cataract surgery, and had follow-up information (including death) for the competing risk models.

SAS (version 9.0, SAS Inc., Cary, NC) was employed for all analyses. Cumulative incidence rates were computed using the competing risk approach, an adaptation of the Kaplan–Meier product limit method, where death and cataract surgery were the competing outcomes.[22] Results are presented for the worse eye. This would be the affected eye when there is a difference between the eyes. If cataract surgery or another condition precluded evaluation of one (or both) eyes, the data for that individual were excluded as of that visit, and the data are censored thereafter. Hazard ratios were estimated using proportional hazard models. Generalized estimating equations were used to evaluate both the continuous relationships of cataract to age and cohort effects, while adjusting for relevant covariates. In these models, a person can contribute information from different examinations. An independent working correlation structure was used for the cohort models.

Age was defined as age at the time of the baseline examination or current age as noted in the text and relevant tables or figures.

from Competing Risk Model (Worse Eye)

Posterior Subcapsular Cataract					Surgery				
N at Risk	*Main Cumulative Incidence*	*HR*	*95% CI*	*P Value*	*N at Risk*	*Main Cumulative Incidence*	*HR*	*95% CI*	*P Value*
637	5.3%				686	5.3%			
518	11.9%	2.8	1.7–4.4	<0.001	584	23.7%	5.5	3.7–8.3	<0.001
505	10.0%	3.4	2.1–5.6	<0.001	597	36.5%	14.0	9.4–20.8	<0.001
195	9.8%	6.3	3.3–11.8	<0.001	282	27.2%	19.4	12.3–30.8	<0.001
1855	8.8%				2149	21.4%			
		1.8	1.5–2.1	<0.001			2.6	2.3–2.9	<0.001
549	4.5%				595	6.0%			
465	9.4%	2.5	1.5–4.3	<0.001	509	13.6%	2.8	1.8–4.4	<0.001
368	11.8%	4.7	2.7–8.0	<0.001	420	25.2%	8.1	5.3–12.5	<0.001
132	6.8%	6.3	2.8–14.3	<0.001	183	10.8%	8.1	4.2–15.4	<0.001
1514	8.0%				1707	13.1%			
		2.0	1.6–2.4	<0.001			2.3	2.0–2.7	<0.001
		1.0	0.7–1.3	0.786			0.7	0.6–0.8	<0.001
1186	4.9%				1281	5.7%			
983	10.7%	2.6	1.9–3.8	<0.001	1093	19.1%	4.2	3.1–5.6	<0.001
873	10.8%	3.9	2.7–5.7	<0.001	1017	31.8%	11.2	8.4–15.0	<0.001
327	8.6%	6.3	3.8–10.4	<0.001	465	20.7%	14.8	10.4–21.2	<0.001
3369	8.4%				3856	17.7%			
		1.8	1.6–2.1	<0.001			2.5	2.3–2.8	<0.001

Results

The 15-year incidence of each of the 3 types of cataract and cataract surgery increases with age in the first 3 age categories but declines in the fourth in the total population (Table 1). The hazard ratios (compared with the incidence in 43- to 54-year-olds) increase for each age category for all cataract end points. Women have higher incident cataract of each type (Table 1), but the sex

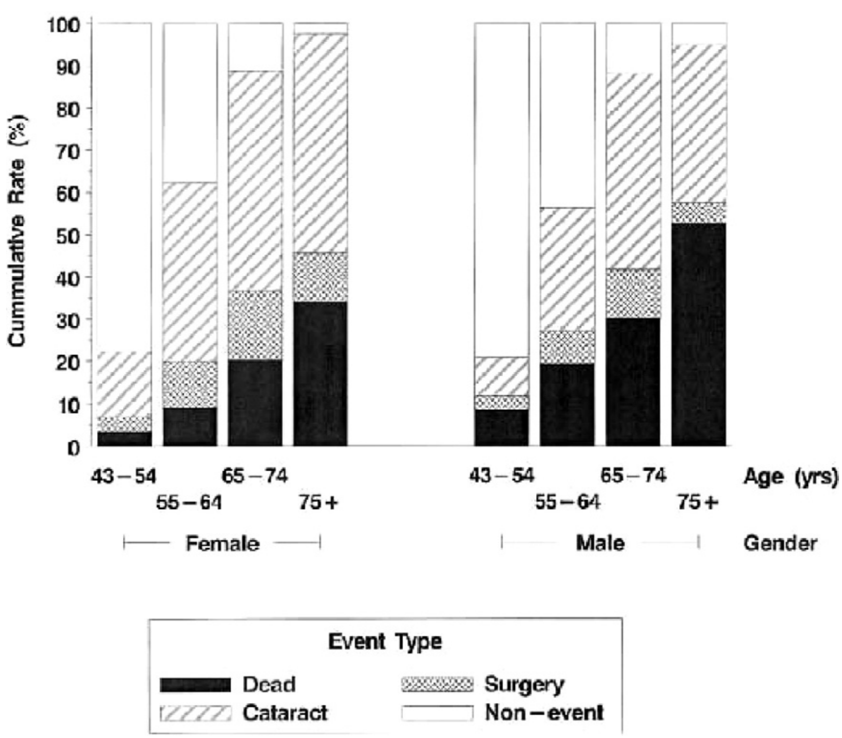

Figure 1. Age and gender distributions of the 15-year cumulative incidence of cataract (worse eye) along with competing events of death and cataract surgery for nuclear cataract.

effect is significant only for nuclear cataract (age-adjusted hazard ratio for men, 0.7 [95% confidence interval (CI), 0.6–0.8]).

The relative effects of the competing risks on incidence estimates are substantial and vary systematically by age group for each type of cataract. Figure 1 displays these data graphically for nuclear cataract, but patterns are similar for cortical cataract and PSC. The effect of mortality increases in each successive age category, but the effect of cataract surgery on these incidence estimates decreases in the last age category for each type of cataract. Men have a higher mortality but less cataract surgery than women.

To assess how age is related to severity of each type of cataract, models were developed with age and severity as continuous measures. Each person contributed multiple times to these general estimating equation models. Predicted values with 95% CIs at each age are shown in Figure 2. The relationship of severity of nuclear sclerosis with age is not linear. It increases with age until age 80 and then appears to plateau. A quadratic model fits better than a

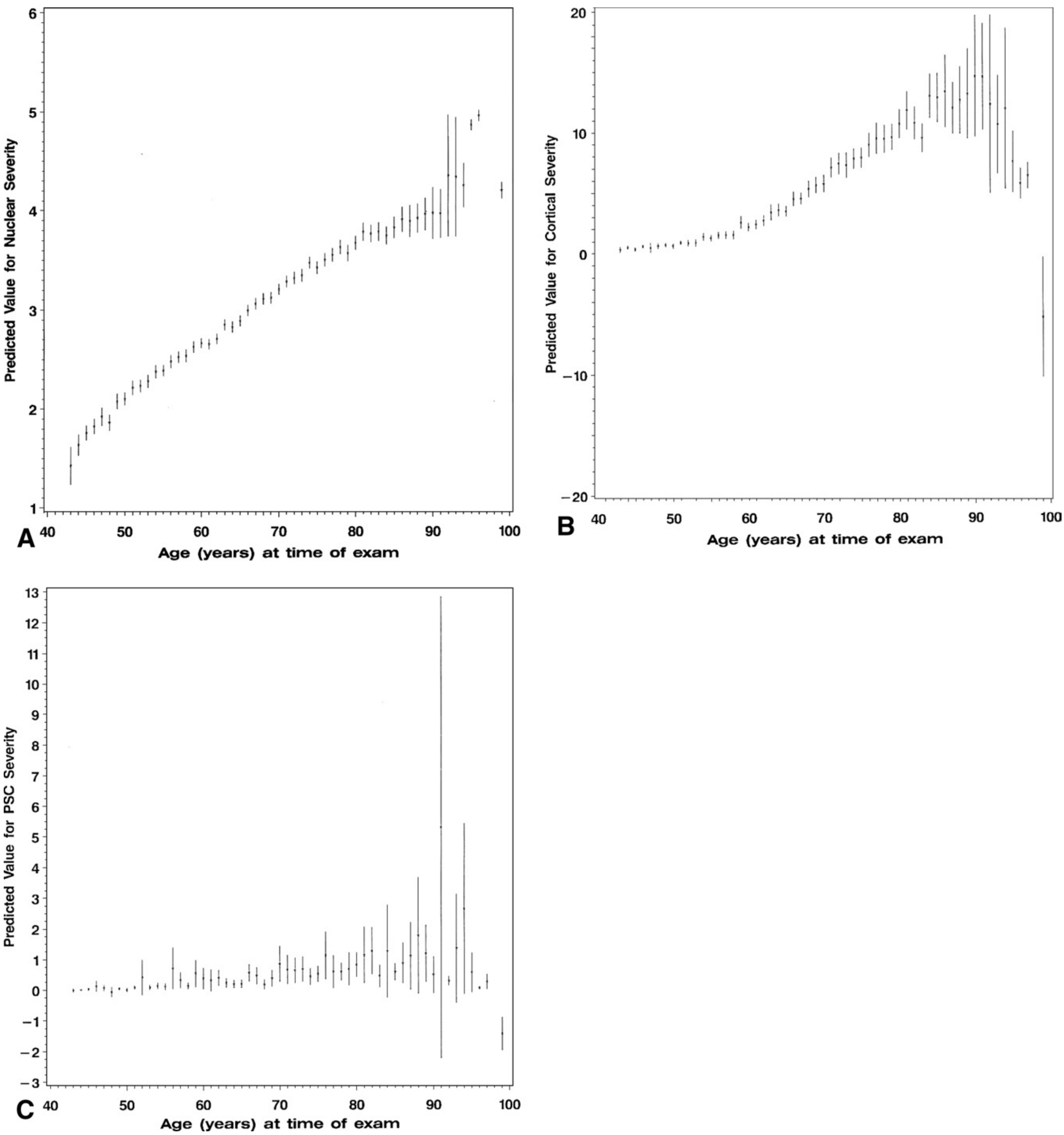

Figure 2. Relationship of age (continuous) to severity of cataract (continuous) for (**A**) nuclear cataract, (**B**) cortical cataract, and (**C**) posterior subcapsular cataract (PSC).

linear model but does not describe the apparent relationship ideally. For cortical opacity (Fig 2B), the relationship is not linear either; a cubic model fits these data better than a quadratic model. For posterior subcapsular opacity, the model appears linear; indeed, neither quadratic nor cubic models improve the fit compared with a linear model (Fig 2).

An apparent age effect could be related to the particular experience of a group of persons born at a given time whose disease frequency reflects different (quality or quantity) environmental exposures earlier in life compared with persons born at other times. To evaluate whether there might be such effects influencing our results, we calculated prevalence and incidence for each cataract type by date of birth in 5-year categories starting with 1898 to 1902 through 1943 to 1947 to compare persons of the same age born at different times. Figure 3 shows these results for prevalent nuclear cataract. Because there were few people in the oldest age groups (earliest birth groups), their data are not displayed. In Figure 3, we see that of 65- to 69-year-olds at the time of the examination, 10.6% (95% CI, 4.9%–16.3%) of those born in 1938 to 1942 (seen at the 2003–2005 examination) had nuclear cataract, whereas 16.2% (95% CI, 12.6%–19.8%) of those born in 1933 to 1937 (seen at the 1998–2000 examination) had nuclear cataract and 27.1% (95% CI, 23.5%–30.8%) of those born in 1923 to 1927 (seen at the 1993–1995 examination) had nuclear cataract. After adjusting for age, we found that a systematic (cohort) effect on nuclear cataract prevalence persists. This effect does not disappear with additional adjustment for gender, income, education, or smoking. Similar analyses were done for other cataract outcomes; we found no significant cohort effects on cortical cataract or PSC (data not shown). We did find a significant effect for cataract surgery such that those of similar ages born in more recent years (or seen at more recent visits) have higher rates of surgery.

We next evaluated whether there was a similar effect on incidence. We found evidence of a cohort effect on 5-year incidence of nuclear cataract, as well as for 5-year incidence of cortical cataract and PSC (data not shown). There was no significant effect on incident cataract surgery (data not shown). Although we are unable to model the cohort effect on 10-year incidence because we need further follow-up data, similar cohort trends seem to be influencing nuclear cataract (data not shown).

Discussion

Incident cataract over a 15-year interval is a frequent occurrence in the Beaver Dam Eye Study cohort. Using the competing events approach, the cumulative risk for nuclear and cortical cataracts at 15 years is >20%, and for PSC, it is >8%. These are more conservative estimates of cumulative rates than the standard Kaplan–Meier calculations produce. Underlying that approach is the assumption that incidence is uniform for all persons (eyes) with missing follow-up data regardless of the reason for its being missing. The latter method yields incidence estimates of 35%, 28%, and 11% for nuclear cataract, cortical cataract, and PSC, respectively (Klein BEK, unpublished data). In this article, we present the competing risks estimates because death and, to a lesser extent, cataract surgery are now frequent occurrences in our population and, in some or many cases, will likely have occurred before a particular cataract type has developed. We have chosen to present these estimates as the primary analyses in this article, unlike in past reports, because with this more aged group, those with missing infor-

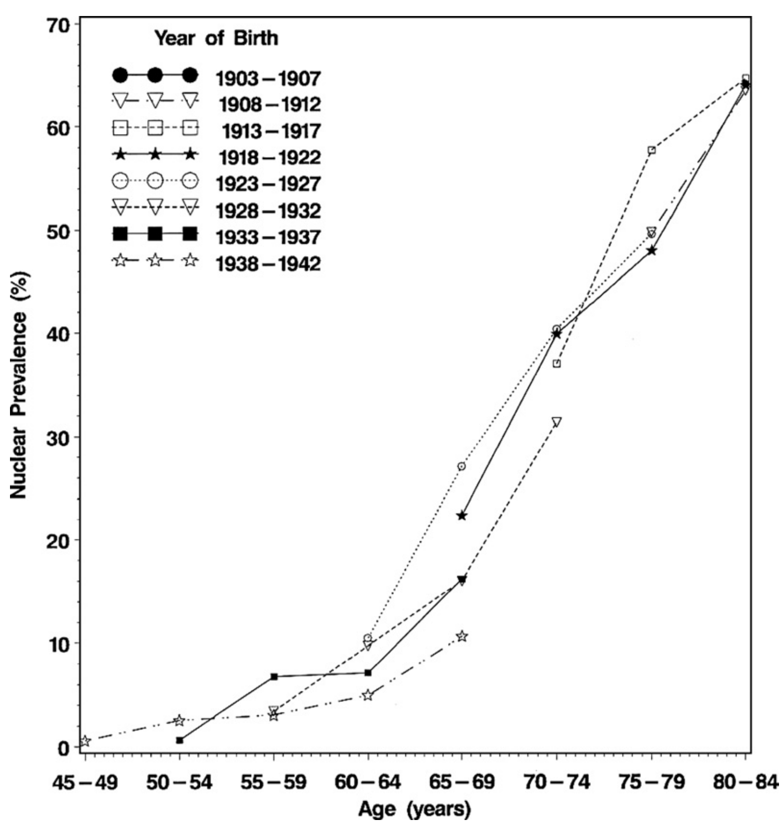

Figure 3. Age and birth cohort distribution of nuclear cataract prevalence.

mation may have had a different incidence than those who had missing data earlier in life, when death and cataract surgery were less common (earlier visits). For example, one cannot have a particular cataract if he or she is dead or if surgery was done for a different type of cataract, whereas one can have cataract if a missed visit was due to having moved away.

Although it is well known that cataract rates increase with age, the specific mathematical model that best represents these relationships has not been described. We found that severity of nuclear and cortical opacities appears to increase nonlinearly with age. Neither a quadratic nor a cubic model improves the fit over a linear model for posterior subcapsular opacity, possibly due to the rarity of PSC. It is likely that cataract surgery has influenced the relationships we observed and may have a greater effect on the relationship for the relatively uncommon posterior subcapsular opacity. We expect that a best-fit model could be important in revealing possible causal relationships.

We detected a cohort effect on prevalence of nuclear cataract at the ages we have studied for the particular birth cohorts in our population. The data for 10-year incidence suggest that such cohort influences may continue in the future. To address this, however, an additional follow-up visit is required. These effects may be due to differences in important exposures before the time that these persons were examined for the prevalence survey or while they have been under our observation. Possible protective exposures include a decrease in smoking and increase in exposure to healthy lifestyle habits, including diet and medication intake.[23] Cohort effects on incidence may permit us to identify some specific antecedents of these trends.

The increase in cataract surgery that we observed is unlikely to reflect increase in frequency of cataract (we found no consistent evidence of such an increase at each period), but rather is a response to improved surgical techniques that make surgery less risky and, therefore, more appealing to persons with milder lens opacities (and to their doctors) than in the past.

In summary, we have found a substantial incidence of 3 types of cataracts and have modeled the varying effects of age on incidence. The risks increase with increasing age despite the influence of mortality and cataract surgery on our data. Although we cannot know the incidences in those lost to follow-up, their influence is likely to be small, as our most common cause of loss to follow-up is death. It is true, however, that populations with different risks of death and surgery may find different estimates of risk due to these factors. In addition, if the distribution of potential protective and causal effects differs in other populations, the apparent decrease in incidence, particularly in nuclear cataract, may not be realized.

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