Age–Period–Cohort Effect on the Incidence of Age-Related Macular Degeneration

The Beaver Dam Eye Study

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Objective: To examine relationships of age, period, and birth cohort with the 5-year incidence of age-related macular degeneration (AMD).

Design: Population-based cohort study with 4 examination visits 5 years apart from 1988 through 1990, 1993 through 1995, 1998 through 2000, and 2003 through 2005.

Participants: Two thousand nine hundred sixty-eight persons (6603 participant visits) and 3588 persons (8184 participant visits) 43 to 86 years of age at baseline contributing to the incidence of early and late AMD, respectively.

Methods: Grading of stereoscopic fundus photographs using the Wisconsin Age-Related Maculopathy Grading System.

Main Outcome Measures: Five-year incidence of early AMD.

Results: While controlling for age, there was a lower 5-year incidence of early AMD in later rather than in earlier birth cohorts (odds ratio per increasing category, 0.70; 95% confidence interval, 0.62–0.78; $P<0.001$). This remained while controlling for smoking, blood pressure, and other related factors. There was no evidence for a period or birth cohort effect with late AMD.

Conclusions: Lower incidence of early AMD in more recent birth cohorts is likely the result of unmeasured risk factors for early AMD. Further study of possible unmeasured risk factors that may have caused this cohort effect may help to identify new modifiable risk factors for AMD. Diminishing incidence of early AMD in later birth cohorts would be expected to result in lower long-term estimates of future incidence of AMD than do current estimates that do not take this effect into account.

Financial Disclosure(s): The authors have no proprietary or commercial interest in any materials discussed in this article. *Ophthalmology 2008;115:1460–1467*

Age-related macular degeneration (AMD) is the most common cause of visual loss in adult white Americans.[1] The prevalence of AMD, based on data from population-based epidemiologic studies, is assumed to be increasing in the United States and elsewhere, in part because of the increasing longevity of the population.[2] Independent of age, other factors, such as cigarette smoking, hypertension, inflammation, multivitamin use, and alcohol consumption, have been shown to be associated with AMD in some, but not all, studies.[3]

Based on 3 examinations of the Beaver Dam cohort, there appeared to be a birth cohort effect for the prevalence of early AMD at the time of the 10-year follow-up not explained by risk factors measured at baseline or in a time-dependent approach.[4] This cohort effect was assumed to be the result of differences in past exposures to unmeasured risk factors. The cohort has been followed up for 15 years. Thus, the authors examined the relationships of age, period, and birth cohort with the 5-year incidence of early and late AMD.

Patients and Methods

Population

Methods used to identify the population and descriptions of the population have appeared in previous reports.[5–9] Of the 5924 enumerated persons 43 to 84 years of age ascertained in a private census from 1987 to 1988, 4926 participated in the baseline examination from 1988 through 1990.[5,6] More than 80% of the surviving eligible group (had AMD assessed in at least 2 successive examinations) has participated in the 5-year (n = 3722), 10-year (n = 2962), and 15-year (n = 2375) follow-up examinations. Comparisons between participants and nonparticipants at each of the examinations appear elsewhere.[6–9]

Procedures

Similar procedures were used at baseline and follow-up examinations.[10–17] Signed informed consent was obtained and Institutional Review Board approval was given by the University of Wisconsin-Madison at the beginning of each examination. Pertinent parts of the examination at both baseline and follow-up examinations consisted of administering a questionnaire to obtain information on

ISSN 0161-6420/08/$–see front matter
doi:10.1016/j.ophtha.2008.01.026

demographic characteristics and physical conditions, using standardized protocols for measuring blood pressure, height, and weight and for taking stereoscopic 30° color fundus photographs centered on the disc (Diabetic Retinopathy Study standard field 1) and macula (Diabetic Retinopathy Study standard field 2) and a nonstereoscopic color fundus photograph temporal to but including the fovea of each eye. Details of the grading procedure have been described previously.[10–12]

Definitions

Definitions of the incidence of early and late AMD have been presented elsewhere.[10–12] In brief, the incidence of early AMD was defined by the presence of either soft indistinct drusen or the presence of retinal pigment epithelium depigmentation or increased retinal pigment together with any type of drusen at follow-up when none of these lesions was present at baseline. The incidence of late AMD was defined by the appearance of either exudative macular degeneration or pure geographic atrophy at follow-up when neither lesion was present at baseline.

The birth cohort (or period) effect was defined as the variation in the incidence of AMD that arose from the different exposures of each birth (period) cohort. In this study, we also were interested in whether the birth (period) cohort effect remained while adjusting for identified risk factors. Birth cohorts were identified categorically by year of birth (1903–1907, 1908–1912, 1913–1917, 1918–1922, 1923–1927, 1928–1932, 1933–1937, 1938–1942). Periods were identified categorically by the calendar year of the initial examination to identify incidence of AMD (1988–1990, 1993–1995, 1998–2000). Similarly, age was identified categorically in 5-year bands of the current age at the initial examination to identify incidence of AMD (43–44, 45–49, 85–89, 90–94 years).

During the examination, a questionnaire was administered to assess history of smoking, drinking, physical activity, and vitamin and medication use. A subject was classified as a current smoker if he or she had smoked more than 100 cigarettes in his or her lifetime and had not stopped smoking, as a former smoker if he or she had smoked more than this number but had stopped smoking, and as a nonsmoker if he or she had smoked fewer than 100 cigarettes in his or her lifetime. Pack years smoked was defined as the average number of cigarettes smoked per day divided by 20, multiplied by the number of years smoked. A current heavy drinker was defined as a person consuming 4 or more servings of alcoholic beverages daily, a former heavy drinker consumed 4 or more servings daily in the past but not in the previous year, and a nonheavy drinker had never consumed 4 or more servings daily on a regular basis. Vitamin use was defined categorically as none, currently taking a single or other combination of vitamins (e.g., B complex), or currently taking a multivitamin. Blood pressure was measured with a random-zero sphygmomanometer according to the Hypertension Detection and Follow-up Program protocol, and the average of the 2 measurements was used for analysis.[13] Mean arterial blood pressure was defined as diastolic pressure + 1/3 (systolic − diastolic blood pressure). Height and body weight were measured with participants wearing light clothing and no shoes. Body mass index was defined as weight in kilograms divided by the height in meters squared. Obesity was defined as body mass index of 30 kg/m^2 or more. Participants were asked if they engaged in a regular activity long enough to work up a sweat. Persons who, on average, did such activities fewer than 3 times weekly were considered to have a sedentary lifestyle. For the purpose of this report, persons were asked to categorize their total household income (<$1000 (K), 1–4K, 5–9K, 10–19K, 20–29K, 30–44K, 45–59K, >60K) and highest year of education achieved (0–11 years, 12 years, 13–15 years, 16+ years).

Statistical Methods

SAS software version 9 was used for analyzing the data (SAS Institute, Inc., Cary, NC). Included in the analyses were 2968 participants (6603 participant-visits) for the incidence of early AMD and 3588 participants (8194 participant-visits) for the incidence of late AMD. Differences in denominators reflected differences in those at risk (for incident early AMD included only persons with no AMD, whereas for late AMD included those with no or early AMD).

Data were structured such that each participant contributed data for 1 to 3 intervals of 5 years, depending on their participation and whether they previously had obtained the AMD outcome. Effects of age, period, and birth cohort were assessed using logistic regression models. Because age, period, and birth cohort are linearly dependent, effects of age, period, and birth cohort are not identifiable in a single model without further assumptions. Age and birth year were categorized into 5-year bands. Pair-wise combination models (age and period, age and birth cohort) were investigated with continuous, categorical, and ordered factor effects. Akaike's information criterion was used to determine the best-fitting model.[18]

Multivariate models were used by including variables that have been shown in other studies to have an effect on period, birth cohort, or AMD. The following were identified as characteristics that may influence the relation between birth (period) cohort and the incidence of AMD: age at the examination, gender, history of smoking status and pack years smoked, heavy alcohol use, vitamin use, sedentary lifestyle, income and education level, mean arterial blood pressure, antihypertensive medication use, and obesity. Interactions were explored between birth cohort and each of these potential confounders by including appropriate interaction terms in the model.

Results

Characteristics of the population at the start of each examination are shown in Table 1. Persons examined at later visits were less likely to have a history of being current smokers or being heavy drinkers, to have less education, and to have less income and were more likely to have lower mean arterial blood pressure and to have a history of using antihypertensive medications than those seen at earlier examinations. The 5-year incidences of early and late AMD are shown by age and birth cohort (Figs 1, 2; Table 2) and age and period (Figs 3, 4; Table 3). For most age groups, there was a lower 5-year incidence of early AMD in later birth cohorts or periods. For example, the 5-year incidence rates of early AMD in people examined when they were 65 to 69 years of age was 14% among those born from 1918 through 1922, 10% among those born from 1923 through 1927, 6% among those born from 1928 through 1932, and 4% among those born from 1933 through 1937.

Models for having age and birth cohort as categorical and, in addition, ordered factor variables are presented in Table 4. The 5-year incidence of early AMD was lower for most later birth cohorts compared with earlier birth cohorts, with the strongest effects seen from 1918 through 1922 versus 1913 through 1917 and 1923 through 1927 compared with the 1918 through 1922 cohorts. Models containing age and birth cohort, both as ordered factor variables, provided the best fit for both early and late AMD. Later birth cohorts had a lower incidence of early AMD (odds ratio [OR], 0.70; 95% confidence interval [CI], 0.62–0.78; $P<0.001$), whereas increasing categories of age were not significantly related to incident early AMD (OR, 1.08; 95% CI, 0.96–1.21; $P = 0.21$). Similar associations were found for 2 lesions characterizing early

Table 1. Characteristics of the Population at the Start of Each Examination Phase

Characteristic	Baseline 1988–1990 (n = 3494), Mean (Standard Deviation)	Beaver Dam Eye Study 2 1993–1995 (n = 2635), Mean (Standard Deviation)	Beaver Dam Eye Study 3 1998–2000 (n = 2067), Mean (Standard Deviation)
Age (yrs)	59.9 (10.2)	63.0 (9.5)	66.4 (8.6)
Gender (% male)	43.9	43.2	41.9
Smoking history (%)			
Past	35.7	39.4	43.0
Current	19.3	13.5	10.4
No. pack years smoked	16.7 (25.4)	15.0 (23.5)	14.7 (23.5)
Heavy drinking history (%)			
Past	14.0	14.9	13.3
Current	2.2	1.9	1.4
Body mass index (kg/m^2)	28.8 (5.4)	29.6 (5.5)	30.2 (5.9)
Mean arterial blood pressure, mmHg	95.4 (11.7)	93.8 (11.7)	93.4 (11.2)
Less than a high school education (%)	23.4	18.7	15.2
Less than $10 000/year household income (%)	12.2	7.5	5.1
Vitamin use			
Single or nonstandard combination	9.0	19.4	21.7
Multivitamin	25.4	29.1	46.0
Sedentary lifestyle (%)	74.0	70.1	70.3
Antihypertensive use (%)	33.4	38.9	50.5

AMD, retinal pigmentary abnormalities and soft indistinct drusen (data not shown). In contrast, birth cohorts were not related to incidence of late AMD (OR, 0.96; 95% CI, 0.78–1.20; $P = 0.74$), whereas age was significantly related to incident late AMD (OR, 1.86; 95% CI, 1.49–2.33; $P<0.001$). Similarly, there was not a significant association of birth cohort, geographic atrophy, and neovascular AMD (data not shown). In models including period as opposed to birth cohort, there was a significant relationship such that persons at later periods had a lower incidence of early AMD than those at earlier periods (data not shown).

Multivariate models for each AMD outcome controlling for potential confounders are shown in Table 5. The birth cohort and age effects did not change much from the unadjusted models. Further controlling for other factors not significantly related to birth cohort (e.g., current smoking) did not affect the results (data not shown). There were no significant interactions between birth cohort and age,

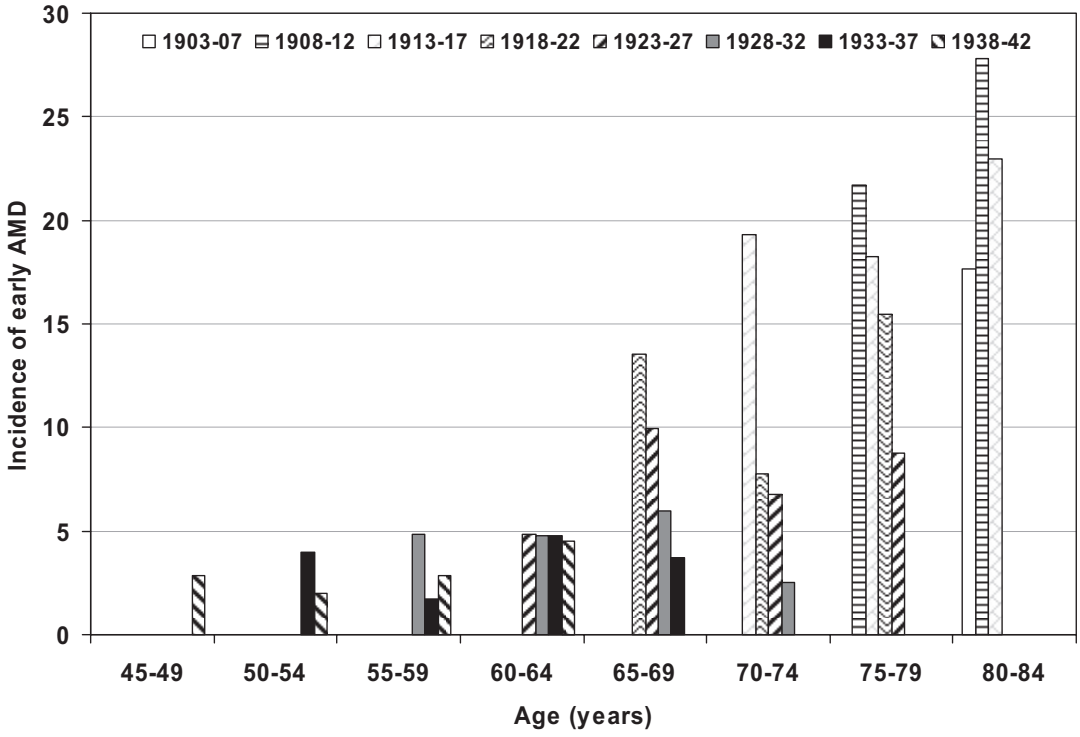

Figure 1. Bar graph demonstrating the 5-year incidence of early age-related macular degeneration (AMD) by age and birth cohort. Data displayed only for subgroups with 30 or more persons. For numbers of persons at risk, see Table 2.

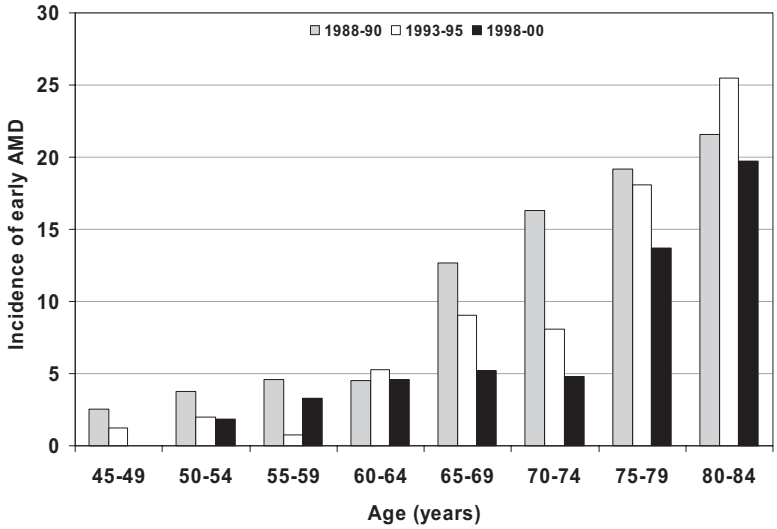

Figure 2. Bar graph demonstrating the 5-year incidence of early age-related macular degeneration (AMD) by age and period cohort. Data displayed only for subgroups with 30 or more persons. For numbers of persons at risk, see Table 3.

Table 2. Five-Year Incidence of Age-Related Macular Degeneration by Age and Birth Year in the Beaver Dam Eye Study

Age (yrs)	Calendar Year of Birth	5-Year Incidence of Early Age-Related Macular Degeneration		5-Year Incidence of Late Age-Related Macular Degeneration	
		No.	%	*No.*	%
45–49	1938–1942	387	2.8	427	0.0
50–54	1933–1937	352	4.0	390	0.0
	1938–1942	506	2.0	566	0.4
55–59	1928–1932	331	4.8	390	0.3
	1933–1937	401	1.7	459	0.0
	1938–1942	416	2.9	461	0.2
60–64	1923–1927	310	4.8	387	0.5
	1928–1932	379	4.7	460	0.7
	1933–1937	335	4.8	381	0.3
	1938–1942	111	4.5	125	0.0
65–69	1918–1922	281	13.5	371	0.3
	1923–1927	361	10.0	461	0.4
	1928–1932	284	6.0	362	1.4
	1933–1937	81	3.7	99	2.0
70–74	1913–1917	197	19.3	279	2.9
	1918–1922	257	7.8	384	2.6
	1923–1927	236	6.8	311	2.3
	1928–1932	79	2.5	95	1.1
75–79	1908–1912	83	21.7	142	3.5
	1913–1917	126	18.3	220	3.6
	1918–1922	149	15.4	212	4.7
	1923–1927	57	8.8	83	1.2
80–84	1903–1907	34	17.6	73	8.2
	1908–1912	54	27.8	104	3.8
	1913–1917	61	23.0	102	6.9
	1918–1922	29	13.8	43	7.0
85–89	1903–1907	12	33.3	33	12.1
	1908–1912	16	31.3	41	7.3
	1913–1917	8	0.0	14	7.1
90–94	1903–1907	1	100.0	5	20.0
	1908–1912	1	0.0	4	25.0

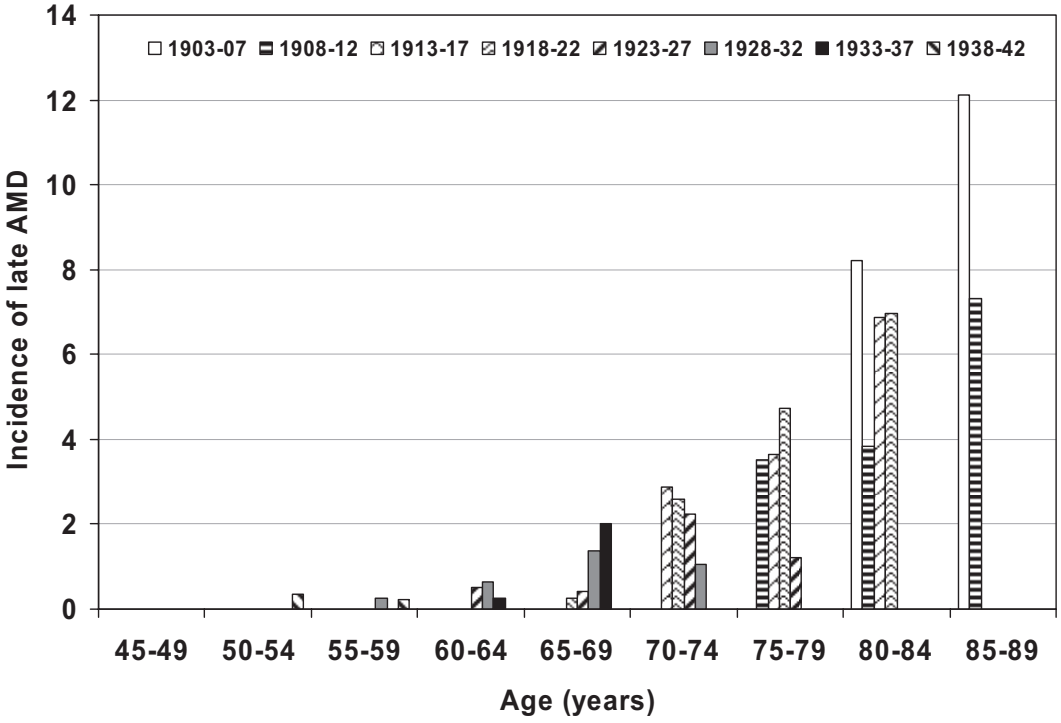

Figure 3. Bar graph demonstrating the 5-year incidence of late age-related macular degeneration (AMD) by age and birth cohort. Data displayed only for subgroups with 30 or more persons. For numbers of persons at risk, see Table 2.

gender, education, smoking, or vitamin or medication use and the incidence of early or late AMD (data not shown).

Discussion

Incidence of AMD often is examined by age strata. One advantage of the long-term study of population-based cohorts with multiple examinations is the opportunity to observe whether birth cohort or period affect this relation. In the Beaver Dam cohort, evidence of lower 5-year incidence of early but not late AMD in later birth and period cohorts was found. This is consistent with earlier finding of a lower prevalence of early AMD in later compared with earlier birth cohorts.[4] To the authors' knowledge, no other studies have examined a cohort effect on incident AMD. There are many possible reasons why persons born in more recent years or seen in later periods have a lower incidence of early

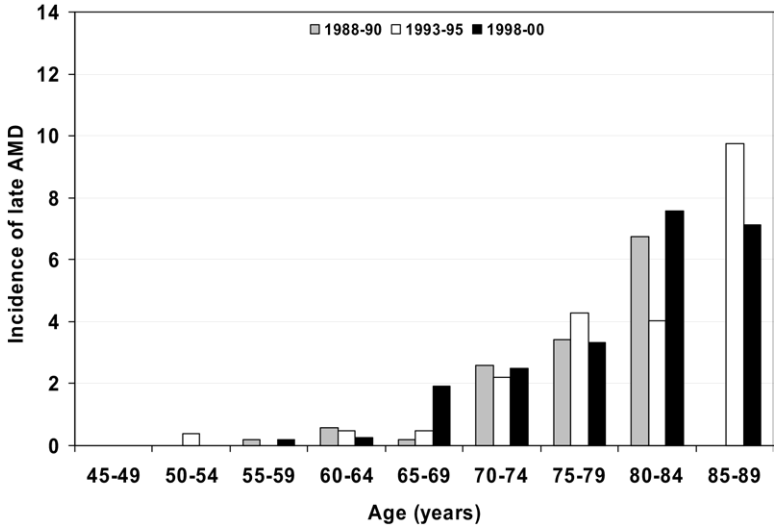

Figure 4. Bar graph demonstrating the 5-year incidence of late age-related macular degeneration (AMD) by age and period. Data displayed only for subgroups with 30 or more persons. For numbers of persons at risk, see Table 3.

Table 3. Five-Year Incidence of Age-Related Macular Degeneration by Age and Time Period in the Beaver Dam Eye Study

Age (yrs)	Year of Started Interval	5-Year Incidence of Early Age-Related Macular Degeneration		5-Year Incidence of Late Age-Related Macular Degeneration	
		No.	%	*No.*	%
<45	1988–1990	88	0.0	91	0.0
45–49	1988–1990	553	2.5	604	0.0
	1993–1995	81	1.2	86	0.0
50–54	1988–1990	500	3.8	554	0.0
	1993–1995	496	2.0	547	0.4
	1998–2000	54	1.9	58	0.0
55–59	1988–1990	434	4.6	510	0.2
	1993–1995	395	0.8	451	0.0
	1998–2000	457	3.3	499	0.2
60–64	1988–1990	421	4.5	519	0.6
	1993–1995	343	5.2	422	0.5
	1998–2000	371	4.6	412	0.2
65–69	1988–1990	387	12.7	511	0.2
	1993–1995	332	9.0	415	0.5
	1998–2000	288	5.2	367	1.9
70–74	1988–1990	270	16.3	387	2.6
	1993–1995	248	8.1	362	2.2
	1998–2000	251	4.8	320	2.5
75–79	1988–1990	120	19.2	205	3.4
	1993–1995	127	18.1	210	4.3
	1998–2000	168	13.7	242	3.3
80–84	1988–1990	51	21.6	104	6.7
	1993–1995	51	25.5	99	4.0
	1998–2000	76	19.7	119	7.6
85–89	1988–1990	3	33.3	7	14.3
	1993–1995	16	25.0	41	9.8
	1998–2000	19	21.1	42	7.1
90–94	1993–1995	1	0.0	2	0.0
	1998–2000	2	50.0	8	25.0

AMD than similarly aged persons born in earlier years or seen in earlier periods. One reason is that persons born at different times or seen in different periods may have differing exposures to factors (e.g., smoking, uncontrolled blood pressure, sedentary lifestyle, intake of multivitamins) and different patterns of care for conditions (e.g., inflammatory or infectious disease) that may affect the incidence of AMD. There may be different levels of vulnerability to such exposures at different times of life or at different stages of AMD. Among risk factors previously reported to be associated with the incidence of AMD, higher mean arterial blood pressure, greater obesity, more frequent history of past heavy drinking, less likelihood of taking vitamins, less income, and less education achieved was found in earlier rather than in later birth cohorts.[3] Many of these findings reflect similar birth cohort effects reported in the United States and elsewhere.[19–22] Less education and lower income in the earlier birth cohorts may be markers for unmeasured lifetime exposures to protective factors (e.g., dietary omega 3s, leafy vegetables) or deleterious factors (e.g., exposure to diets with high glycemic index or diets high in saturated fats) that may account, in part, for the birth cohort effect found. However, when added to multivariable models, mean arterial blood pressure and education or income level resulted in no attenuation of the cohort effect. The effect of childhood and young adult exposures to infectious and inflammatory diseases (e.g., flu epidemic in 1918), patterns of cigarette smoke inhalation and characteristics of cigarette type smoked (tar, nicotine content), or dietary deprivation during periods like the Great Depression in the 1930s and their effect on the incidence of AMD in different birth cohorts cannot be evaluated. Furthermore, birth cohort effects cannot be differentiated from period effects.

Current forecasts of 25-year estimates of prevalent early AMD are based on the assumption that the earlier observed trends will be similar in future years.[2] However, this assumption may not be correct if decreasing incidence of AMD continues with each new birth cohort as observed in the Beaver Dam Eye Study cohort. Lower prevalence of AMD may be expected in the future because current estimates are based on existing data and do not take into account possible drops in incidence as more recently born cohorts age.

The current study, with AMD measured objectively from fundus photographs obtained at 4 examinations 5 years apart in a large population-based cohort, provides data on the cohort effect for this condition. Nevertheless, the results from this study should be interpreted with caution. First, the study participants were white. Therefore, the results from this study may not apply to other racial or ethnic groups. Second, the current analysis was limited to participants who remained alive during each of the 5-year intervals of follow-up. It is possible that risk factors (e.g., education, diet, smoking) may have differentially affected the relationship between participation and mortality and incidence of AMD

Table 4. Age and Birth Cohort Models for Incidence of Early and Late Age-Related Macular Degeneration

Contrast	Incidence of Early Age-Related Macular Degeneration		Incidence of Late Age-Related Macular Degeneration	
	Odds Ratio (95% Confidence Interval)	P *Value*	*Odds Ratio (95% Confidence Interval)*	P *Value*
Age (yrs)				
50–54 vs. 45–49	0.91 (0.42–1.94)	0.80	CNE	
55–59 vs. 50–54	0.97 (0.56–1.69)	0.91	0.72 (0.09–5.49)	0.75
60–64 vs. 55–59	1.26 (0.79–2.03)	0.33	3.31 (0.61,17.88)	0.16
65–69 vs. 60–64	1.44 (0.98–2.13)	0.07	1.76 (0.58–5.34)	0.31
70–74 vs. 65–69	0.68 (0.47–0.97)	0.03	3.20 (1.45–7.07)	0.004
75–79 vs. 70–74	1.32 (0.91–1.94)	0.15	1.55 (0.85–2.83)	0.15
80–84 vs. 75–79	1.10 (0.68–1.77)	0.70	1.60 (0.81–3.15)	0.18
85–89 vs. 80–84	1.07 (0.46–2.49)	0.88	1.50 (0.62–3.62)	0.37
90–94 vs. 85–89	0.34 (0.02–5.97)	0.46	0.37 (0.06–2.11)	0.26
Age-ordered factor	1.08 (0.96–1.21)	0.21	1.86 (1.49–2.33)	<0.001
Year of birth				
1908–1912 vs. 1903–1907	1.16 (0.52–2.62)	0.72	0.58 (0.24–1.40)	0.23
1913–1917 vs. 1908–1912	0.86 (0.53–1.40)	0.54	1.33 (0.63–2.79)	0.46
1918–1922 vs. 1913–1917	0.53 (0.36–0.77)	<0.001	0.98 (0.53–1.78)	0.94
1923–1927 vs. 1918–1922	0.63 (0.44–0.90)	0.01	0.70 (0.34–1.46)	0.35
1928–1932 vs. 1923–1927	0.72 (0.49–1.07)	0.10	1.75 (0.71–4.32)	0.23
1933–1937 vs. 1928–1932	0.79 (0.50–1.26)	0.32	0.60 (0.15–2.51)	0.49
1938–1942 vs. 1933–1937	1.21 (0.72–2.02)	0.47	0.59 (0.10–3.29)	0.54
Birth year-ordered factor*	0.70 (0.62–0.78)	<0.001	0.96 (0.78–1.20)	0.74

CNE = Cannot estimate.
*Ordered factor effects were fit using the categorical variable as a linear effect in a separate model.

in different birth cohorts. The authors have not observed evidence of differences in participation among those at risk of AMD in the different birth and period cohorts, making it less plausible that this would explain the reduction of incident AMD in later birth and period cohorts. Third, the power to detect an age-birth cohort and period effects for late AMD is somewhat limited by the low incidence of this outcome.

In summary, the authors found that persons born in more recent years or examined in a later period have a lower 5-year incidence of early AMD than similarly aged persons born earlier or examined in an earlier period. Observed differences in health care changes (e.g., better control of blood pressure, use of antihypertensive agents) and lifestyle changes (e.g., less smoking) over the previous 15 years do not explain these findings. It is not clear whether other

Table 5. Multivariate Generalized Estimating Equation Models for 5-Year Incidence of Early and Late Age-Related Macular Degeneration

	Incidence of Early Age-Related Macular Degeneration		Incidence of Late Age-Related Macular Degeneration	
	Odds Ratio (95% Confidence Interval)	P *Value*	*Odds Ratio (95% Confidence Interval)*	P *Value*
Age-ordered factor	1.06 (0.94–1.20)	0.32	1.37 (1.04–1.82)	0.03
Birth year-ordered factor	0.70 (0.62–0.79)	<0.001	0.96 (0.74–1.26)	0.78
Male gender	0.88 (0.69–1.11)	0.27	0.85 (0.49–1.48)	0.56
Education-ordered factor	0.86 (0.76–0.96)	0.01	0.94 (0.73–1.19)	0.59
Pack years smoked per 10 years	1.03 (0.99–1.08)	0.16	1.05 (0.95–1.15)	0.34
Mean arterial blood pressure per 10 mmHg	0.92 (0.83–1.01)	0.06	0.89 (0.74–1.08)	0.25
BMI per 10 kg/m^2	1.06 (0.96–1.18)	0.22	1.26 (1.03–1.54)	0.03
Vitamin use				
Multivitamin vs never	0.87 (0.68–1.11)	0.25	0.97 (0.56–1.68)	0.91
Single/combination vs never	1.01 (0.75–1.37)	0.93	0.97 (0.53–1.76)	0.91
History of heavy drinking				
Current vs. never	1.29 (0.58–2.88)	0.54	2.45 (0.62–9.73)	0.20
Past vs. never	0.79 (0.55–1.14)	0.21	0.64 (0.27–1.50)	0.31
Baseline AMD severity			7.26 (5.49–9.59)	<0.001

AMD = age-related macular degeneration; BMI = body mass index.

exposures earlier in life (e.g., infectious disease outbreaks such as the flu pandemic of 1918), dietary restrictions specific to a period (e.g., the Great Depression), or other unmeasured factors during later life may explain these birth cohort and period differences. Regardless, birth cohort and period effects should be monitored and taken into account when projecting estimates of future prevalence of AMD.

References

1. Eye Diseases Prevalence Research Group. Causes and prevalence of visual impairment among adults in the United States. Arch Ophthalmol 2004;122:477-85.
2. Eye Diseases Prevalence Research Group. Prevalence of age-related macular degeneration in the United States. Arch Ophthalmol 2004;122:564-72.
3. Klein R, Peto T, Bird A, Vannewkirk MR. The epidemiology of age-related macular degeneration. Am J Ophthalmol 2004; 137:486–95.
4. Huang GH, Klein R, Klein BE, Tomany SC. Birth cohort effect on prevalence of age-related maculopathy in the Beaver Dam Eye Study. Am J Epidemiol 2003;157:721–9.
5. Linton KL, Klein BE, Klein R. The validity of self-reported and surrogate-reported cataract and age-related macular degeneration in the Beaver Dam Eye Study. Am J Epidemiol 1991;134:1438–46.
6. Klein R, Klein BE, Linton KL, De Mets DL. The Beaver Dam Eye Study: visual acuity. Ophthalmology 1991;98:1310–5.
7. Klein R, Klein BE, Lee KE. Changes in visual acuity in a population: the Beaver Dam Eye Study. Ophthalmology 1996; 103:1169–78.
8. Klein R, Klein BE, Lee KE, et al. Changes in visual acuity in a population over a 10-year period: the Beaver Dam Eye Study. Ophthalmology 2001;108:1757–66.
9. Klein R, Klein BE, Lee KE, et al. Changes in visual acuity in a population over a 15-year period: the Beaver Dam Eye Study. Am J Ophthalmol 2006;142:539–49.
10. Klein R, Klein BE, Jensen SC, Meuer SM. The five-year incidence and progression of age-related maculopathy: the Beaver Dam Eye Study. Ophthalmology 1997;104:7–21.
11. Klein R, Klein BE, Tomany SC, et al. Ten-year incidence and progression of age-related maculopathy: the Beaver Dam Eye Study. Ophthalmology 2002;109:1767–79.
12. Klein R, Klein BE, Knudtson MD, et al. Fifteen-year cumulative incidence of age-related macular degeneration: the Beaver Dam Eye Study. Ophthalmology 2007;114:253–62.
13. Klein R, Klein BE. The Beaver Dam Eye Study: Manual of Operations (Revised). Springfield, VA: National Technical Information Service; 1991:74-112. NTIS Accession No. PB91-149823.
14. Klein R, Klein BE. The Beaver Dam Eye Study II. Manual of Operations. Springfield, VA: National Technical Information Service; 1995:61-90. NTIS Accession No. PB95-273827.
15. Klein R, Davis MD, Magli YL, et al. The Wisconsin Age-Related Maculopathy Grading System. Ophthalmology 1991; 98:1128–34.
16. Klein R, Davis MD, Magli YL, et al. Wisconsin Age-Related Maculopathy Grading System. Springfield, VA: National Technical Information Service; 1991:8-46. NTIS Accession No. PB91-184267.
17. Klein R, Klein BE, Linton KL. Prevalence of age-related maculopathy: the Beaver Dam Eye Study. Ophthalmology 1992;99:933–43.
18. Akaike H. Information theory and the extension of the maximum likelihood principle. In: Petrov BN, Csadki F, eds. 2nd International Symposium on Information Theory. Budapest, Hungary: Akadémiai Kiadó; 1973:267–81.
19. Vartiainen E, Jousilahti P, Alfthan G, et al. Cardiovascular risk factor changes in Finland, 1972–1997. Int J Epidemiol 2000;29:49–56.
20. Flegal KM, Carroll MD, Ogden CL, Johnson CL. Prevalence and trends in obesity among US adults, 1999–2000. JAMA 2002;288:1723–7.
21. Moore AA, Gould R, Reuben DB, et al. Longitudinal patterns and predictors of alcohol consumption in the United States. Am J Public Health 2005;95:458–65.
22. Ding J, Kritchevsky SB, Newman AB, et al. Effects of birth cohort and age on body composition in a sample of community-based elderly. Am J Clin Nutr 2007;85:405–10.

Footnotes and Financial Disclosures

Originally received: September 19, 2007.
Final revision: January 24, 2008.
Accepted: January 28, 2008. Manuscript no. 2007-1222.

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Financial Disclosure(s):
The authors have no proprietary or commercial interest in any materials discussed in this article.

Supported by the National Institutes of Health, Bethesda, Maryland (grant no. EY06594 [RK, BEKK]), and in part by Senior Scientific Investigator Awards from Research to Prevent Blindness, Inc., New York, New York (RK, BEKK). The National Eye Institute provided funding for the entire study, including collection and analyses of data; Research to Prevent Blindness provided further additional support for data analyses.

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