Incidence of Exudative Age-Related Macular Degeneration among Elderly Americans

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Purpose: To estimate the 3-year incidence of exudative age-related macular degeneration (AMD) and its treatment by laser photocoagulation in elderly Americans.

Design: Population-based cohort study using insurance claims data.

Participants: A random 5% sample of Medicare beneficiaries, age 65 and older.

Methods: Incidence of exudative AMD and of laser photocoagulation for this condition was assessed based on four categories of ascertainment criteria that included procedure and diagnosis codes associated with exudative AMD, choroidal neovascularization, and its treatment.

Main Outcome Measures: Incidence of AMD and of associated laser photocoagulation.

Results: Overall, the 3-year incidence of exudative AMD is estimated to be between 9.4 per 1000 and 11.4 per 1000 Americans age 65 and older (depending on ascertainment criteria), based on those diagnosed and treated by ophthalmologists for the condition. These estimates bracket the measured incidence of exudative AMD in the Beaver Dam Eye Study and lie within its 95% confidence interval. The 3-year incidence of exudative AMD with attendant laser photocoagulation was 2.3 per 1000. Women were found to have a slightly higher incidence of AMD than men using all ascertainment criteria ($P < 0.001$), and white Americans were found to have a fivefold-to-sixfold higher ascertainment criteria than black Americans ($P < 0.001$).

Conclusions: The reported incidence of exudative AMD identified in the population of Medicare beneficiaries suggests that measurements on incidence for this condition derived from the Beaver Dam Eye Study can be generalized to the U.S. population. *Ophthalmology 2003;110:1534–1539 © 2003 by the American Academy of Ophthalmology.*

Age-related macular degeneration (AMD) is believed to be the most common cause of irreversible vision loss in the elderly population. Although prevalence of AMD and related vision loss has been measured in multiple studies,[1,2] only two population-based studies have reported incidence of AMD in the United States. One published study reports AMD incidence from a sample of 3583 participants of Beaver Dam, Wisconsin.[3] The second reports the incidence of choroidal neovascularization from a relatively small sample (n = 483) of Chesapeake Bay area residents, half of whom were younger than 50 years of age.[4] This latter study uses an opportunistic sampling strategy, and many of the initially sampled participants were excluded from the 5-year incidence study because they had either died or were unable to complete the fundus photographs. Most of the other estimates of annual incidence of late AMD have been based on persons attending ophthalmologic or specialty clinics.

Another means of estimating incidence of AMD, particularly exudative AMD (or its pathologic manifestations of choroidal neovascularization and pigment epithelial detachment), is by analysis of insurance claims. This approach suffers from obvious sources of bias and confounding (see Discussion) and is more likely to identify persons with more clinically advanced AMD. However, insurance claims analysis may be useful for assessing the generalizability of more precise, but geographically localized, cross-sectional studies. Because the vast majority of individuals with AMD are 65 or older, Americans with AMD are likely to be covered by the Medicare program. The use of the Medicare database, both for general health care research[5] and for the study of ophthalmologic conditions,[6–9] has been described in detail previously. The Medicare database provides the unique advantage of a representative sample of the U.S. population. Although it has numerous limitations (see Discussion), epidemiologic estimates derived from this source provide useful comparisons to those obtained from less representative, but more rigorously characterized, populations.

Population and Methods

Five years (1994–1998) of the 5% sample of Medicare medical claims data from the Standard Analytical File were used to develop

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Table 1. Diagnosis and Procedure Codes Used for Ascertainment of Age-related Macular Degeneration

"Diagnostic test" (B) is defined by CPT4 codes 92230, 92235, 92240, 92250.
"Office visit or eye exam" (A) is defined by CPT4 codes 92002, 02004, 92012, 92014, 92225, 92226, and 99201–99354.
Diagnosis codes for exudative age-related macular degeneration 362.52, 362.42, and 362.43.
Photocoagulation is defined by CPT4 codes 67210 and 67228.
Ophthalmologist: type of provider identified in Medicare claim, "18."

CPT = Current Procedural Terminology, version 4.

Table 2. Ascertainment Criteria Used to Identify Exudative Age-related Macular Degeneration in the Medicare Database

Criterion	CPT Codes Required for Ascertainment	Provider Type Required for Ascertainment
Laser	Photocoagulation for AMD	Ophthalmologist
Level 1	Two office visits for exudative AMD or one office visit and one diagnostic test	Retinal specialist (see Table 3)
Level 2	Two office visits for exudative AMD or one office visit and one diagnostic test	Ophthalmologist
Level 3	A single office visit for exudative AMD	Ophthalmologist

AMD = Age-related macular degeneration; CPT = Current Procedural Terminology, version 4.

a longitudinal study cohort. This file is prepared annually by the Centers for Medicare and Medicaid (formerly the Health Care Financing Administration), based on the last two digits of the beneficiary's social security number. A period from 1994 to 1995 was defined as the "prebaseline" period, and a period from 1996 through 1998 as the study period. As is common practice, beneficiaries who were members of Medicare Health Maintenance plans were excluded, because incomplete data are available about their care. Similarly, those enrolled in Medicare before age 65 because of disability or end-stage renal disease were excluded because they are not representative of the U.S. population.

Potential cases of exudative AMD were ascertained using diagnosis (ICD-9) and procedure (CPT-4) codes contained in the claims file (Table 1). There is clear potential for inconsistency across eye care providers in the accuracy of diagnosis coding. Therefore, we established several ascertainment criteria for AMD with decreasing levels of specificity (Table 2), but with corresponding increases in sensitivity, as has been done in similar studies. The least specific criterion was a single diagnosis of exudative AMD appearing on an ophthalmologist claim. The most specific criterion was a claim for laser photocoagulation of exudative AMD.

A component of the ascertainment criteria depends on whether the ophthalmologist filing the claim is a retinal specialist or a nonretinal specialist. The concern is that retinal specialists may have more specific criteria for classifying a patient as having exudative AMD, whereas nonretinal specialists may be more likely to enter exudative AMD as a "rule- out" diagnosis. Because retinal specialists are not identified either in the claims data or in any known directory that can be mapped to the claims data, we analyzed the surgical and laser procedure claims submitted by all ophthalmologists treating Medicare beneficiaries and characterized those claims by whether they were for retinal procedures. We then characterized all ophthalmologists by overall volume of surgery and by the percent of surgery that was retina related. As can be seen in Table 3, we made an empirical classification of ophthalmologists into retinal specialists and nonretinal specialists. The retinal specialists include 2086 ophthalmologists who collectively perform 69% of all retinal procedures in Medicare beneficiaries. This classification was based on the actual case mix of the physician's practice and may or may not correspond to having completed fellowship training in retinal disease.

Based on the above ascertainment criteria, the 3-year incidence of AMD was defined as the proportion of beneficiaries who met one of those criteria during the study period and who did not meet any of those criteria during the baseline period (1994 and 1995). To adjust for the impact of patient mortality before the end of the follow-up period, the Kaplan-Meier method was used to estimate incidence. A subanalysis was performed to test the validity of 2-year baseline period by identifying those patients treated in the 1994–95 baseline period, not treated in the subsequent 2 years, but treated again in 1998. To explore the demographic aspects of exudative AMD incidence, we examined 3-year incidence by 5-year age group (65–69, 70–74, 75–79, 80–84, and 85+), by gender and by race (white vs. black). We also compared our estimates with those of the Beaver Dam Study.

Statistical analysis was performed using SAS software (The SAS Institute, Cary, NC). Confidence intervals around the point estimate of incidence were calculated using the normal distribution.

Table 3. Ascertainment Criteria for Retinal Specialists

Total Eye Procedures	Percent of Ophthalmologist's Surgical Practice Devoted to Retinal Procedures					
	0%–1%	*1%–25%*	*26%–50%*	*51%–75%*	*76%–100%*	*Total*
20–60	1681 (11.5%)	41 (0.3%)	146 (1.0%)	85 (0.6%)	0 (0%)	1953 (13.4%)
61–100	706 (4.9%)	91 (0.6%)	36 (0.3%)	14 (0.1%)	61 (0.4%)	908 (6.2%)
101–600	3927 (27.0%)	1560 (10.7%)	283 (2.0%)	160 (1.1%)	557 (3.8%)	6487 (44.5%)
601–1000	974 (6.7%)	947 (6.5%)	81 (0.6%)	32 (0.2%)	310 (2.1%)	2344 (16.1%)
1000+	958 (6.6%)	1454 (10.0%)	93 (0.6%)	50 (0.3%)	324 (2.2%)	2879 (19.8%)
Total	8246 (56.6%)	4093 (28.1%)	639 (4.4%)	341 (2.3%)	1252 (8.6%)	14.571 (100%)

Shaded region denotes ophthalmologists classified as "retinal specialists" for the purpose of this analysis.

Table 4. Three-year Incidence of Age-related Macular

Sex and Age	Laser					Level 1				
	No. at Risk	*No. with Wet Age-related Macular Degeneration*	*Incidence %*	*95% Confidence Interval*		*No. at Risk*	*No. with Wet Age-related Macular Degeneration*	*Incidence %*	*95% Confidence Interval*	
				Lower	*Upper*				*Lower*	*Upper*
Men										
65–69	145,359	159	0.12	0.10	0.13	145,257	313	0.22	0.20	0.25
70–74	118,982	237	0.21	0.19	0.24	118,863	343	0.31	0.27	0.34
75–79	77,925	244	0.35	0.30	0.39	77,845	381	0.54	0.48	0.59
80–84	39,709	130	0.39	0.32	0.46	39,629	186	0.53	0.45	0.61
85+	17,835	43	0.30	0.21	0.39	17,807	73	0.50	0.38	0.61
Total	399,810	813	0.22	0.21	0.24	399,401	1,296	0.35	0.33	0.37
Women										
65–69	187,519	222	0.12	0.10	0.14	187,407	362	0.20	0.18	0.22
70–74	170,764	402	0.25	0.22	0.27	170,584	631	0.38	0.35	0.41
75–79	132,413	423	0.35	0.31	0.38	132,153	651	0.52	0.48	0.56
80–84	88,447	263	0.33	0.29	0.37	88,274	451	0.56	0.51	0.62
85+	60,537	137	0.27	0.22	0.31	60,409	183	0.35	0.30	0.40
Total	639,680	1,447	0.24	0.23	0.25	638,827	2,278	0.38	0.36	0.39
Total										
65–69	332,878	381	0.12	0.11	0.13	332,664	675	0.21	0.19	0.22
70–74	289,746	639	0.23	0.21	0.25	289,447	974	0.35	0.33	0.37
75–79	210,338	667	0.35	0.32	0.37	209,998	1,032	0.53	0.50	0.56
80–84	128,156	393	0.35	0.31	0.38	127,903	637	0.55	0.51	0.60
85+	78,372	180	0.28	0.23	0.32	78,216	256	0.38	0.33	0.43
Total	1,039,490	2,260	0.23	0.22	0.24	1,038,228	3,574	0.37	0.35	0.38

Results

A total of 1,041,009 Medicare beneficiaries met the enrollment criteria and were followed up in the study. As shown in Table 4, the 3-year estimated incidence of exudative macular degeneration in the Medicare population ranges from 0.37% (95% confidence interval [CI], 0.35, 0.38) to 1.14% (95% CI, 1.12, 1.16), depending on the ascertainment criteria chosen. The 3-year incidence of photocoagulation for presumed exudative AMD is 0.23% (95% CI, 0.22, 0.24).

We compared the incidence estimated from the Medicare data with that reported by Klein et al from the Beaver Dam Eye Study. Extrapolating from the published report, the 5-year incidence of exudative AMD in persons aged 65 and older is 1.48% (95% CI, 0.80%, 2.16%). Because the published age ranges do not coincide precisely with our age range of interest, the authors have kindly confirmed the accuracy of this estimate (Klein R, personal communication, 2002). If the 3-year incidence we measured is adjusted in a linear fashion to approximate a 5-year incidence, the estimates for level 2 and level 3 ascertainment criteria fall within the 95% CI around the Beaver Dam incidence figure (Fig 1).

Clearly, the estimate of incidence is dependent on valid ascertainment of disease-free status at baseline. Because we relied on the absence of a diagnosis of exudative AMD during the 2-year baseline period for our definition of disease-free status, it is important to attempt to test the robustness of this measure. We investigated the effect of extending the baseline window to 3 years rather than 2 years. Our analysis suggested that approximately 4% of incident cases would be eliminated by such an extension. Because this small additional specificity would not affect the conclusions of the study but would reduce the available treatment window from 3 years down to 2, given the available data, we decided that the 2-year baseline window was appropriate.

As shown in Figure 2, the incidence of exudative AMD increases linearly with age, but seems to level off at the oldest age group. There is no biological basis to suggest a decrease in true incidence. However, it may well be that decreasing mobility and other, more acute medical needs make it less likely that the oldest beneficiaries seek and obtain care for exudative AMD. In fact, a cross-sectional study of cause-specific blindness in the nursing home population of Baltimore determined that nursing home residents were several times more likely to be blind or visually impaired than their noninstitutional-dwelling cohorts. A major cause of blindness among nursing home residents was AMD.[10]

We examined the relative incidence of exudative AMD in men and women and found increasingly greater incidence among women relative to men as the sensitivity of the ascertainment criteria increased (Fig 3). After adjustment for age, all gender differences in incidence are statistically significant ($P < 0.05$).

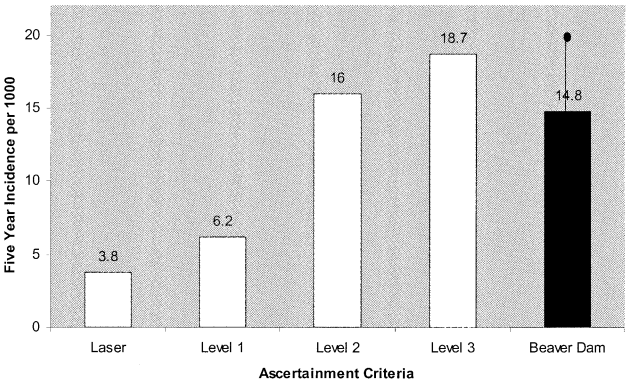

Figure 1. A comparison between the extrapolated incidence of exudative age-related macular degeneration (AMD) in the Medicare population and the 5-year incidence in Beaver Dam residents who were more than 65 years of age at baseline. Exudative AMD incidence estimates based on level 2 and level 3 ascertainment criteria in our study fall within the 95% confidence interval around the Beaver Dam incidence figure. The 95% confidence limit around the extrapolated incidence in the Medicare population is approximately ± 0.3 per 1000 (not shown for clarity).

Degeneration by Age and Ascertainment Criteria

Level 2					Level 3				
	No. with Wet Age-related Macular		*95% Confidence Interval*			*No. with Wet Age-related Macular*		*95% Confidence Interval*	
No. at Risk	*Degeneration*	*Incidence %*	*Lower*	*Upper*	*No. at Risk*	*Degeneration*	*Incidence %*	*Lower*	*Upper*
145,061	690	0.50	0.46	0.54	144,992	781	0.57	0.53	0.61
118,547	882	0.80	0.75	0.86	118,411	1,007	0.92	0.86	0.98
77,435	931	1.36	1.27	1.45	77,281	1,068	1.56	1.47	1.66
39,362	536	1.63	1.49	1.77	39,261	656	1.99	1.84	2.15
17,693	210	1.54	1.33	1.75	17,634	268	1.99	1.75	2.24
398,098	3,249	0.89	0.86	0.93	397,579	3,780	1.04	1.01	1.08
187,109	889	0.49	0.46	0.52	186,987	1,043	0.57	0.54	0.61
170,007	1,559	0.96	0.91	1.00	169,844	1,785	1.09	1.04	1.14
131,420	1,627	1.34	1.28	1.41	131,167	1,957	1.62	1.55	1.69
87,610	1,222	1.59	1.50	1.68	87,340	1,509	1.98	1.88	2.08
60,003	593	1.20	1.10	1.30	59,783	773	1.58	1.47	1.69
636,149	5,890	1.00	0.97	1.02	635,121	7,067	1.20	1.17	1.22
332,170	1,579	0.49	0.47	0.52	331,979	1,824	0.57	0.54	0.60
288,554	2,441	0.89	0.86	0.93	288,255	2,792	1.02	0.98	1.06
208,856	2,558	1.35	1.29	1.40	208,448	3,025	1.60	1.54	1.66
126,972	1,758	1.60	1.53	1.68	126,601	2,165	1.98	1.90	2.07
77,696	803	1.28	1.19	1.37	77,417	1,041	1.67	1.57	1.77
1,034,247	9,139	0.96	0.94	0.98	1,032,700	10,847	1.14	1.12	1.16

Age-related macular degeneration and particularly exudative AMD are also known to be much more common in white persons, as contrasted with black persons. For all ascertainment levels, exudative AMD was approximately fivefold more common in white Medicare beneficiaries than in their black counterparts (Fig 4).

Discussion

Overall, the results obtained in this study are consistent with previous studies of AMD incidence in local populations and suggest that those findings are generalizable to the rest of the United States population. Given the potential biases and limitations inherent in the use of claims data for estimating incidence, the most striking finding of this study may be how close the claims data-derived estimates are to those estimates derived using precise, validated epidemiologic techniques. The claims data-derived estimates fall within the 95% CI reported in the population-based study.

In this study, we have attempted to measure the 3-year per-person incidence, as opposed to the per-eye incidence of exudative AMD. Choroidal neovascularization in the fellow eye of an already-affected individual is a common phenomenon, occurring at an annual rate of approximately 9% to 10% among those in whom exudative AMD has developed already in the first eye.[11] The lack of information on laterality in the Medicare database makes it impossible to estimate the incidence of exudative AMD per eye.

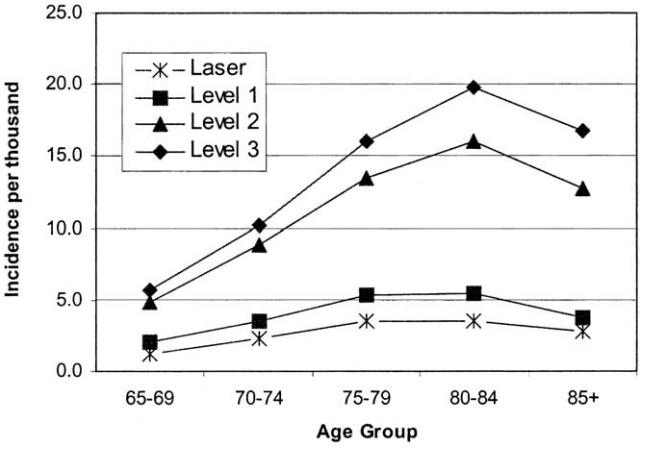

Figure 2. The 3-year incidence of exudative age-related macular degeneration is shown categorized by age at baseline and ascertainment criteria. The 95% confidence intervals around estimates are shown in Table 4.

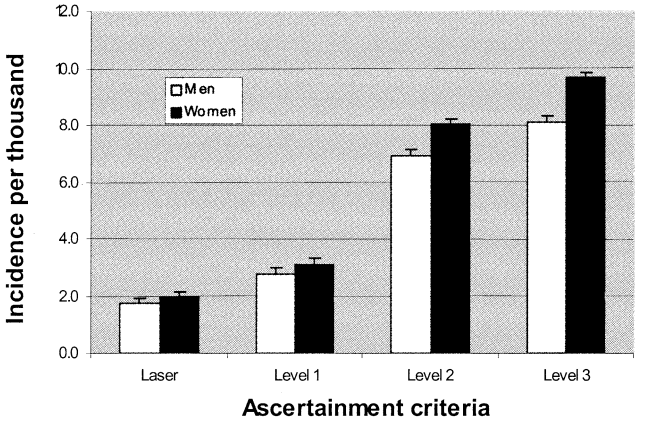

Figure 3. The 3-year incidence of exudative age-related macular degeneration with 95% confidence intervals (error bar) demonstrates a statistically significant difference ($P < 0.001$) between men and women.

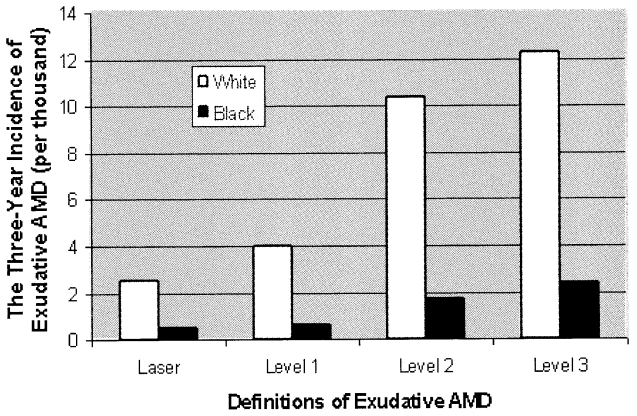

Figure 4. Three-year incidence of exudative age-related macular degeneration by race and ascertainment criteria.

Use of the Medicare dataset in this manner has one overwhelming advantage, as compared with other epidemiologic techniques, but many limitations. The obvious advantage is that the sampling frame of the Medicare database includes nearly all elderly Americans. The limitations include referral bias and ascertainment bias and may be confounded further by issues of access to care. These issues are discussed in considerable detail by Coleman and Morgenstorn.[9]

Nearly all Medicare claims-based studies, including those in the area of eye care,[6–9] exclude the approximately 5% of Medicare beneficiaries who are enrolled in Medicare + Choice (HMO) plans. This exclusion is necessitated by the lack of detailed encounter information available on these individuals, unlike those in Medicare fee-for-service in whom every physician, hospital, and laboratory encounter is reported. Approximately 20% of Medicare beneficiaries aged 65 to 74 years and 18% of beneficiaries aged 75 to 85 years join Medicare HMOs.[12] To the extent that persons with AMD are more or less likely as a result of their condition to join a Medicare HMO, our results may be affected by selection bias. A major motivating factor for patients to join an HMO, which generally involves trading off choice of physician and hospital in return for reduced copayments and pharmacy benefits, is the need for prescription drugs on a regular basis. Although some chronic diseases, such as glaucoma, may provide patients with a financial incentive to join an HMO, there is no particular reason to believe that AMD would have this effect.

In contrast to the previous epidemiologic studies of AMD incidence, there are no clear clinical criteria in the International Classification of Diseases taxonomy for recording a diagnosis of exudative AMD. The diagnosis, like nearly all ICD-9 diagnoses, is left to clinical judgment. Moreover, previous authors have shown that primary diagnosis is, at best, 90% accurate in the context of a careful chart review. We believe that the ascertainment criteria used in this study are increasingly specific, though decreasingly sensitive, from level 3 through "Laser."

Although diagnosis codes are supposed to be based on the actual examination findings, there is widespread belief that they are also used to indicate suspicion of specific clinical entities as a basis for justifying the level of examination performed (i.e. "rule-out" diagnoses). Accordingly, we believe that a coded diagnosis of AMD can be accorded greater credence when it is accompanied by a laboratory test for the same entity or by a second office visit with the same code. Similarly, we believe it likely that a code for exudative AMD entered by an ophthalmologist who devotes a significant proportion of his or her practice to retinal procedures is likely to be more specific than the same code entered by an ophthalmologist whose practice is more general in nature.

Ideally, a validation study ought to be conducted in which the diagnostic coding of patients with AMD is compared with the medical record and with retinal photographs, read by a validated reading center. This may yield a classification scheme for claims data studies that is more sensitive and specific than the coding taxonomies we used.

The ascertainment of exudative AMD in the epidemiologic studies was based on standardized photographs read by a small group of highly trained and standardized readers. Hence, there was little room for interobserver variation. In our study, AMD was ascertained by approximately 14,000 ophthalmologists who, obviously, have different individual criteria for assigning the diagnosis and likely have some variability in thoroughness of examination and diagnostic acumen.

In the epidemiologic studies, there was a clear attempt to survey an entire population, with various means for encouraging nonresponders to participate. In our study, the only members of the population able to be ascertained as having exudative AMD were those who obtained ophthalmologic care. However, AMD is not a silent disease. Those experiencing AMD-related visual loss are likely to be motivated to seek care. Nevertheless, barriers to accessing care, inherent either to the health system or to the patient's personal situation, will lead to underascertainment. This is likely the case for the most elderly of beneficiaries, who are more likely to be homebound, to have decreased mobility, and to have competing medical conditions that make eye care less of a priority for them.

The slightly higher incidence of exudative AMD in women, as compared with men, also was seen in the Beaver Dam Study. It is known that women, in general, receive more care for other eye conditions, such as cataract and glaucoma, under Medicare. Although there may be a biological difference worthy of further exploration, it is also possible that women are more likely to seek and to receive care for AMD, along with other eye conditions.

The preponderance of white Americans among those ascertained with AMD is consistent with all previous reports of the relation between race and AMD. Some may find it surprising that the observed incidence ratio of white to black Americans, approximately 5:1, was not higher because fewer than 1.5% of patients meeting the entry criteria for the Macular Photocoagulation Study were black.[13] The low incidence of exudative AMD among blacks is similarly suggested by the Baltimore Eye Study, which showed that the proportion of blindness attributable to AMD was 30% among white persons but 0% among black persons.[14] Although the race indicator in the Medicare data is known to

be based on imperfect, self-identified criteria, our findings may suggest that there is slightly more exudative AMD than has been suspected among the black population.

Despite the potential limitations inherent in attempting to measure disease incidence from administrative claims data, we believe that this paper provides a basis for extending the findings of more precise, but more localized, epidemiologic studies to the broader population. Our findings confirm that exudative AMD is a sight-threatening condition that annually affects upward of 0.3% of the Medicare-age population 65 years and older each year. Therefore, new treatments designed to prevent vision loss related to exudative AMD stand to benefit hundreds of thousands of elderly Americans.

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