Rates of Nonexudative and Exudative Age-Related Macular Degeneration among Asian American Ethnic Groups

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PURPOSE. To determine whether the risk for nonexudative and exudative age-related macular degeneration (AMD) varies for Americans of different Asian ethnicities.

METHODS. Claims data from a large national United States managed care network were reviewed to identify Asian Americans age 40 and older who had ≥ 1 eye care visits from 2001 to 2007. International Classification of Disease (ICD-9CM) billing codes were used to identify enrollees with nonexudative and exudative AMD. Incidence and prevalence rates were calculated for nonexudative and exudative AMD and were stratified by Asian ethnicity. Cox regression analyses were performed to determine the relative risk for developing nonexudative and exudative AMD for persons of different Asian ethnicities, with adjustment for sociodemographic factors and ocular and medical conditions.

RESULTS. Of the 44,103 Asian Americans who met the inclusion criteria, 2221 (5.04%) had nonexudative AMD and 217 (0.49%) had exudative AMD. Chinese Americans (adjusted hazard ratio [HR], 1.63; 95% confidence interval [CI], 1.50–1.77) and Pakistani Americans (HR, 1.97, 95% CI, 1.40–2.77) had a significantly increased risk for nonexudative AMD compared with non-Hispanic white Americans. By contrast, Japanese Americans had a 29% decreased risk for nonexudative AMD compared with non-Hispanic white Americans (HR, 0.71; 95% CI, 0.59–0.85). There were no significant differences in risk for exudative AMD for any of the Asian ethnicities compared with white Americans.

CONCLUSIONS. Asian Americans are the second fastest growing racial group in the United States. Eye care providers must be aware of the overall disease burden of AMD within this group and appreciate how disease rates can vary substantially among different Asian ethnicities. (*Invest Ophthalmol Vis Sci.* 2011; 52:6842–6848) DOI:10.1167/iovs.11-7179

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Presented at the annual meeting of the Association for Research in Vision and Ophthalmology, Fort Lauderdale, Florida, May 2010.

Supported by National Eye Institute K23 Mentored Clinician Scientist Award (JDS; EY019511), Blue Cross Blue Shield of Michigan Foundation (JDS), an unrestricted grant from Research to Prevent Blindness, a Research to Prevent Blindness Lew R. Wasserman Merit Award (DCM), and a Research to Prevent Blindness Sybil B. Harrington Special Scholar Award for Macular Degeneration (DNZ).

Submitted for publication January 6, 2011; revised March 24 and May 30, 2011; accepted July 10, 2011.

Disclosure: **J.D. Stein**, None; **B.L. VanderBeek**, None; **N. Talwar**, None; **B. Nan**, None; **D.C. Musch**, None; **D.N. Zacks**, None

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Age-related macular degeneration (AMD) is the most common cause of visual impairment among adults aged 60 and older in the United States.¹ More than seven million Americans are affected by AMD.² The number of Americans older than 55 years is expected to grow from 70 million in 2008 to 96 million by 2020, with many of these persons at risk for chronic eye diseases such as AMD.^{3,4} In a recent study of 2,259,061 enrollees in a large US managed care network, 60-year-old Asian Americans were at 28% increased risk for nonexudative AMD compared with similarly aged white Americans.⁵ Given that Asian Americans are the second-fastest growing US minority, with nearly two million Asian Americans older than 60 years, we sought to identify whether persons of specific Asian ethnicities are more likely than others to develop AMD. Such findings would increase clinicians' awareness of Asian American subgroups potentially at increased risk for AMD and would be helpful for health policy makers in deciding whom to target for AMD screening and interventions.

Although several studies have looked at AMD prevalence in different Asian countries,^{6–9} we know of only one study that has examined AMD rates among Americans of Asian ethnicity. Using data from the Multi-Ethnic Study on Atherosclerosis (MESA) study, Klein et al.¹⁰ found that Chinese Americans had a reduced risk for early AMD, but an increased risk for late AMD, compared with white Americans. The present study seeks to further our understanding of the epidemiology of nonexudative and exudative AMD among persons of different Asian ethnicities in a large group of Asian Americans residing in communities throughout the United States. Furthermore, we evaluated the risk for AMD among persons of specific Asian ethnicities to determine whether the risks are similar among them.

METHODS

The University of Michigan Institutional Review Board (IRB) determined this study was exempt from requiring IRB approval given that the data are completely deidentified.

Data Source

The i3 InVision Data Mart database (Ingenix, Eden Prairie, MN) contains deidentified records of all beneficiaries in a large US managed care network. We analyzed a subset of beneficiaries who had any form of eye care from January 1, 2001, through December 31, 2007. The subset consisted of patients with ≥ 1 International Classification of Diseases¹¹ (ICD-9CM) codes for any eye-related diagnosis (360–379.9) or Current Procedural Terminology¹² (CPT-4) code for any eye-related visits, diagnostic or therapeutic procedures (65,091–68,899 or 92,002–92,499), or any other ICD-9CM or CPT codes assigned by an ophthalmologist or optometrist during their time in the medical plan. For each beneficiary in the sample, we had access to all medical claims

(inpatient, outpatient, skilled nursing facility) for ocular and nonocular medical conditions. The database also contains detailed demographic (age, sex, race, ethnicity) and socioeconomic (education level, household net worth) information.

Sample Selection

All persons aged 40 and older who had ≥ 1 visit to an eye care provider and were in the database for ≥ 1 consecutive year were identified. Those in the plan for ≤ 365 days or who had noncontinuous enrollment were excluded (Fig. 1). Two sources were used by the managed care company to identify race and ethnicity: public records (drivers license data) and E-Tech (Ethnic Technologies, South Hackensack, NJ), a tool that uses information from the beneficiary name and the census block to assign race and ethnicity. Previous comparisons between information collected by patient self-report and assignment of race using E-Tech demonstrated that E-Tech has a positive predictive value of 71%,¹³ and information from the company indicates this software actually has a 96% accuracy at correctly classifying patients based on race and ethnicity.¹⁴ Patients of Asian American descent were identified, and each was classified by ethnicity: Chinese, Filipino, Indian, Japanese, Korean, Pakistani, and Vietnamese. There were inadequate numbers of Bangladeshi, Burmese, Laotians, Thai, Indonesians, Malaysians, Hawaiians, Samoans, and Sri Lankans to study these groups separately. Those of these ethnicities were classified as "other."

Incidence and Prevalence

ICD-9CM codes were used to determine whether each beneficiary had ≥ 1 diagnosis of nonexudative AMD (ICD-9CM codes 362.50, 362.51, and 362.57) or exudative AMD (362.52) during their time in the medical plan. Incidence and prevalence rates were determined for both AMD types. Beneficiaries were counted in the disease incidence and prevalence estimates for each AMD type they were documented to have; thus, each enrollee could have more than one form of AMD during their time in the plan. The database does not contain information to allow specification of eye laterality. Participants could have nonexudative AMD in one eye and exudative AMD in the other eye and thus be counted in both groups. Prevalence rates of nonexudative and

exudative AMD were obtained by identifying the number of persons diagnosed with each condition divided by the number of beneficiaries in the medical plan from 2001 to 2007. When interpreting prevalence estimates, it is important to note that not every beneficiary was in the plan for all 7 years and that the period prevalence estimates generated are not directly comparable with point prevalence estimates generated from cross-sectional studies. Incidence rates of nonexudative and exudative AMD were calculated by dividing the number of newly diagnosed beneficiaries with each AMD type by their time, in person-years, in the plan at risk. Diagnoses were considered incident cases if the enrollee had no record of the AMD type of interest during their first year in the plan. Using the rate ratio test, unadjusted nonexudative and exudative AMD incidence, and prevalence rates for the different Asian ethnicities were compared with rates for non-Hispanic white Americans, the reference group.

Statistical Analysis

Analyses were performed using commercial software (SAS 9.2; SAS Institute, Cary, NC). Participant characteristics were summarized for the entire sample using means and standard deviations for continuous variables and frequencies and percentages for categorical variables. Incidence and prevalence estimates were generated for nonexudative and exudative AMD and stratified according to Asian ethnicity.

Cox regression models were developed to determine the relative risk for nonexudative and exudative AMD.¹⁵ For these models, we used the first year of each beneficiary's enrollment in the plan as a look-back period. To avoid selection bias, follow-up of all enrollees started at 1 year after enrollment. Those diagnosed with nonexudative or exudative AMD during the look-back period (nonincident cases) were excluded. Persons were followed up until they developed the event (nonexudative or exudative AMD) or were censored (either when they left the medical plan or the last day for which we had data: December 31, 2007). For each beneficiary, the age to event or the age to censoring was determined. Using age as the time axis and Asian ethnicity as the key predictor of interest, the Cox model was left-truncated at the age of index (1 year after entry into the medical plan). The assumption of proportional hazards required for Cox regression modeling was

FIGURE 1. Sample selection criteria.

checked, and it was verified that there was no violation of this assumption, which meant that the relative risk for AMD for each Asian ethnicity group did not vary by age. Adjustments were made for age, sex, region of residence, education level, household net worth, and the following medical and ocular conditions: diabetes mellitus, hypertension, hyperlipidemia, obesity, myocardial infarction, congestive heart failure, peripheral vascular disease, cerebrovascular accident, renal insufficiency, coagulopathy, blood-loss anemia, deficiency anemias, systemic hypotension, skin cancer (a surrogate measure of long-term sun exposure), cataract, pseudophakia or aphakia, diabetic retinopathy, and open-angle glaucoma (Table 1). $P < 0.05$ was considered statistically significant.

RESULTS

Of the 2,259,061 beneficiaries who met the inclusion criteria, 1923,752 (85.2%) were classified according to ethnicity. Among these, 44,103 (2.3%) were classified as of an Asian ethnicity. Median age at entry into the plan for the overall sample was 52 years (range, 40–87 years). For white Americans, the median age was 52 years; for Asian Americans it was 50 years.

Prevalence and Incidence Rates of AMD

Among persons of all races who met the eligibility criteria, there were 113,234 cases of nonexudative AMD, for an overall

prevalence of 5.01%. The prevalence of nonexudative AMD in white Americans was 5.40%; among Asian Americans as a whole, it was 5.04%. Among Asian Americans, Chinese Americans had the highest prevalence of nonexudative AMD (6.50%), followed by Korean Americans (5.19%), Pakistani Americans (4.90%), Filipino Americans (4.77%), Japanese Americans (4.36%), Vietnamese Americans (4.21%), and Indian Americans (3.54%). The rate ratio test, which was used to compare the unadjusted prevalence of nonexudative AMD for each Asian ethnicity with the prevalence in white Americans, showed significantly lower prevalence rates of nonexudative AMD in Japanese Americans, Vietnamese Americans, and Indian Americans. Chinese Americans were the only Asian ethnicity to have a significantly higher prevalence rate of nonexudative AMD than white Americans (Table 2).

Among persons of all races, there were 69,521 incident cases of nonexudative AMD, for an overall incidence of 1.16%. The incidence of nonexudative AMD among white patients (1.18%) was similar to that of Asian patients (1.17%). Compared with white Americans, Chinese Americans (1.56%) and Pakistani Americans (1.32%) each had a higher incidence of nonexudative AMD, and Korean Americans (1.17%), Filipino Americans (1.14%), Vietnamese Americans (0.97%), Japanese Americans (0.96%), and Indian Americans (0.81%) each had a lower incidence. The rate ratio test confirmed that the unadjusted incidence rate was

TABLE 1. ICD-9CM Codes Used in the Analysis

Nonexudative AMD	362.50, 362.51, 362.57
Exudative AMD	362.52
Cataract	366, 366.0, 366.00, 366.01, 366.02, 366.03, 366.04, 366.09, 366.1, 366.10, 366.12, 366.13, 366.14, 366.15, 366.16, 366.17, 366.18, 366.19, 366.41, 366.45
Diabetes mellitus	250.0, 250.00, 250.01, 250.02, 250.03, 250.1, 250.10, 250.11, 250.12, 250.13, 250.2, 250.20, 250.21, 250.22, 250.23, 250.3, 250.30, 250.31, 250.32, 250.33, 250.4, 250.40, 250.41, 250.42, 250.43, 250.5, 250.50, 250.51, 250.52, 250.53, 250.5, 250.50, 250.51, 250.52, 250.53, 250.6, 250.60, 250.61, 250.62, 250.63, 250.7, 250.70, 250.71, 250.72, 250.73, 250.8, 250.80, 250.81, 250.82, 250.83, 250.9, 250.90, 250.91, 250.92, 250.93, 362.01, 362.02, 362.03, 362.04, 362.05, 362.06, 362.07
Diabetic retinopathy	362.01, 362.02, 362.03, 362.04, 362.05, 362.06, 362.07
Hyperlipidemia	272, 272.0, 272.1, 272.2, 272.3, 272.4, 272.5, 272.6, 272.7, 272.8, 272.9
Hypertension	401, 401.0, 401.1, 401.9, 405, 405.0, 405.1, 405.01, 405.09, 405.11, 405.19, 405.9, 405.91, 405.99, 362.11, 402, 402.0, 402.00, 402.01, 402.1, 402.10, 402.11, 402.9, 402.90, 402.91, 403, 403.0, 403.00, 403.01, 403.1, 403.10, 403.11, 403.9, 403.90, 403.91, 404.0, 404.00, 404.01, 404.02, 404.03, 404.1, 404.10, 404.11, 404.12, 404.13, 404.9, 404.90, 404.91, 404.92, 404.93
Open-angle glaucoma	365.1, 365.10, 365.11, 365.12, 365.15
Obesity	278.0, 278.00, 278.01, 278.02
Pseudophakia or aphakia	V43.1, 379.3, 379.31
Blood-loss anemia	280.0
Deficiency anemias	280.1, 280.8, 280.9, 281.x, 281.0, 281.1, 281.2, 281.3, 281.4, 281.8, 281.9
Congestive heart failure	398.91, 402.01, 402.11, 402.91, 404.01, 404.03, 404.11, 404.13, 404.91, 404.93, 425.4, 425.5, 425.7, 425.8, 425.9, 428.x, 428.0, 428.1, 428.2, 428.20, 428.21, 428.22, 428.23, 428.3, 428.30, 428.31, 428.32, 428.33, 428.4, 428.40, 428.41, 428.42, 428.43, 428.9
Myocardial infarction	410.x, 410.0, 410.00, 410.01, 410.02, 410.1, 410.10, 410.11, 410.12, 410.2, 410.20, 410.21, 410.22, 410.3, 410.30, 410.31, 410.32, 410.4, 410.40, 410.41, 410.42, 410.5, 410.50, 410.51, 410.52, 410.6, 410.60, 410.61, 410.62, 410.7, 410.70, 410.71, 410.72, 410.8, 410.80, 410.81, 410.82, 410.9, 410.90, 410.91, 410.92, 412.x
Cerebrovascular disease	362.34, 430.x, 431.x, 432.x, 432.0, 432.1, 432.9, 433.x, 433.0, 433.1, 433.2, 433.3, 433.8, 433.9, 434.x, 434.0, 434.00, 434.01, 434.1, 434.10, 434.11, 434.9, 434.90, 434.91, 435.x, 435.0, 435.1, 435.2, 435.3, 435.8, 435.9, 436.x, 437.x, 437.0, 437.1, 437.2, 437.3, 437.4, 437.5, 437.6, 437.7, 437.8, 437.9, 438.x, 438.0, 438.1, 438.10, 438.11, 438.12, 438.19, 438.2, 438.20, 438.21, 438.22, 438.3, 438.30, 438.31, 438.32, 438.4, 438.40, 438.41, 438.42, 438.5, 438.50, 438.51, 438.52, 438.53, 438.6, 438.7, 438.8, 438.81, 438.82, 438.83, 438.84, 438.85, 438.89, 438.9
Peripheral vascular disease	093.0, 437.3, 440.x, 440.0, 440.1, 440.2, 440.20, 440.21, 440.22, 440.23, 440.24, 440.29, 441.x, 441.0, 441.00, 441.01, 441.02, 441.03, 441.1, 441.2, 441.3, 441.4, 441.5, 441.6, 441.7, 441.9, 443.1, 443.2, 443.21, 443.22, 443.23, 443.24, 443.29, 443.8, 443.81, 443.82, 443.89, 443.9, 447.1, 557.1, 557.9, V434
Renal disease	403.01, 403.11, 403.91, 404.02, 404.03, 404.12, 404.13, 404.92, 404.93, 582.x, 582.0, 582.1, 582.2, 582.4, 582.8, 582.81, 582.89, 582.9, 583.0, 583.1, 583.2, 583.4, 583.6, 583.7, 585.x, 585.1, 585.2, 585.3, 585.4, 585.5, 585.5, 585.6, 585.9, 586.x, 588.0, V42.0, V45.1, V56, V56.0, V56.1, V56.2, V56.3, V56.31, V56.32, V56.8
Coagulopathies	286.x, 286.0, 286.1, 286.2, 286.3, 286.4, 286.5, 286.6, 286.7, 286.9, 287.1, 287.3, 287.30, 287.31, 287.32, 287.33, 287.39, 287.4, 287.5
Hypotension	458.x, 458.0, 458.1, 458.2, 458.21, 458.29, 458.8, 458.9
Skin cancer	172.x, 172.1, 172.2, 172.3, 172.4, 172.5, 172.6, 172.7, 172.8, 172.9, 17.3, 173.0, 173.1, 173.2, 173.3, 173.4, 173.5, 173.6, 173.7, 173.8, 173.9

TABLE 2. Incidence and Prevalence of Nonexudative and Exudative AMD by Asian Ethnicity

Strata	N	Nonexudative AMD						Exudative AMD					
		Prevalence			Incidence			Prevalence			Incidence		
		n	Rate (%)	Ratio	95% CI	n	Rate (%)	n	Rate (%)	Ratio	95% CI	n	Rate (%)
Overall	225,9061	113,234	5.01			69,521	1.16	17,181	0.76			10,635	0.17
Ethnicity													
Non-Asian Whites	1,535,008	82,818	5.40			51,886	1.18	12,857	0.84			8,100	0.18
Vietnamese	5,420	228	4.21	0.78*	0.68-0.89	142	0.97	19	0.35	0.42*	0.27-0.66	13	0.09
Japanese	4,771	208	4.36	0.81*	0.71-0.93	136	0.96	28	0.59	0.70	0.48-1.02	18	0.12
Chinese	15,918	1,035	6.50	1.21*	1.13-1.28	635	1.56	82	0.52	0.62*	0.49-0.76	50	0.12
Filipino	2,514	120	4.77	0.88	0.74-1.06	79	1.14	22	0.88	1.04	0.69-1.59	14	0.20
Korean	3,948	205	5.19	0.96	0.84-1.10	125	1.17	23	0.58	0.70	0.46-1.05	14	0.13
Indian	8,312	294	3.54	0.66	0.58-0.74	187	0.81	35	0.42	0.50	0.36-0.70	23	0.10
Pakistani	1,000	49	4.90	0.91	0.69-1.20	35	1.32	2	0.20	0.24*	0.06-0.95	1	0.04
Other Asian	2,220	82	3.69	0.68*	0.55-0.85	56	0.92	6	0.27	0.32*	0.14-0.72	1	0.02

Ethnicity was unknown for 335,309 persons.

* $P < 0.05$.

higher for Chinese Americans and lower for Vietnamese Americans, Japanese Americans, and Indian Americans than for white Americans (Table 2).

In the overall sample, among all races, there were 17,181 cases of exudative AMD, yielding a prevalence rate of 0.76%. The prevalence of exudative AMD was 0.84% in white Americans. Only Filipino Americans had a higher prevalence rate of exudative AMD (0.88%), though this difference was insignificant. Vietnamese Americans, Chinese Americans, Pakistani Americans, and Indian Americans had significantly lower prevalence rates of exudative AMD than white Americans. Similar findings were observed when comparing the incidence rate ratios among the Asian ethnicities (Table 2).

Multivariable Analyses

After adjustment for sociodemographic and clinical variables, Pakistani Americans had a 97% increased risk for nonexudative AMD (hazard ratio [HR], 1.97 95% confidence interval [CI], 1.40-2.77), and Chinese Americans had a 63% increased risk for nonexudative AMD (HR, 1.63; 95% CI, 1.50-1.77) compared with white Americans. Japanese Americans had a 29% decreased risk for nonexudative AMD (HR, 0.71; 95% CI, 0.59-0.85) than white Americans. There was no significant difference in the risk for nonexudative AMD when comparing each of the other Asian ethnicities to white Americans. None of the Asian ethnicities had a significantly different risk for exudative AMD than white Americans (Table 3). Supplementary Table S1 (<http://www.iovs.org/lookup/suppl/doi:10.1167/iovs.11-7179/-DCSupplemental>) shows results of a multivariate analysis assessing the risk for nonexudative and exudative AMD for each of the different Asian ethnicities compared with Chinese Americans (rather than white Americans). Aside from Pakistani Americans, all other Asian ethnicities had lower risk for nonexudative AMD than Chinese Americans. There were no differences in the risk for exudative AMD among each Asian ethnicity relative to Chinese Americans.

Survival functions tell the likelihood of surviving (i.e., not receiving a diagnosis of the AMD type of interest) among those at risk at different ages. At all ages, Japanese Americans had a lower likelihood for nonexudative AMD, and Chinese Americans had a higher likelihood for nonexudative AMD than did white Americans, and these differences became more pronounced with increasing age (Fig. 2). Across age ranges, the likelihood for exudative AMD was similar for each of the Asian ethnicities compared with that for white Americans (Fig. 3).

The fact that ICD-9CM code 362.50 is not specific for exudative or nonexudative AMD could have led to the misclassification of some enrollees. We ran a sensitivity analysis, excluding from the regression models all persons diagnosed with AMD, using billing code 362.50 exclusively and found no significant differences (results not shown) from those presented in the models described.

DISCUSSION

We identified significant differences in the risk for nonexudative AMD among the Asian American ethnic groups examined. Compared with white Americans, Chinese and Pakistani Americans were at higher risk for nonexudative AMD, whereas Japanese Americans were at reduced risk for nonexudative AMD. In contrast, rates of exudative AMD were relatively similar among white Americans and the various Asian American ethnic groups.

Comparison with Other US Studies

Little has been known about the risk for AMD among persons of Asian ancestry residing in the United States. We know of

TABLE 3. Univariate and Multivariable HRs for Nonexudative and Exudative AMD by Ethnicity

	Univariate Analyses				Multivariable Analyses			
	Nonexudative AMD		Exudative AMD		Nonexudative AMD		Exudative AMD	
	HR	95% CI	HR	95% CI	HR	95% CI	HR	95% CI
Vietnamese	1.19*	1.01-1.41	0.90	0.52-1.56	1.15	0.96-1.38	0.70	0.37-1.35
Japanese	0.77*	0.65-0.92	0.67	0.42-1.06	0.71*	0.59-0.85	0.64	0.40-1.04
Chinese	1.73*	1.59-1.87	0.94	0.71-1.25	1.63*	1.50-1.77	0.95	0.71-1.27
Filipino	1.10	0.89-1.38	1.36	0.80-2.29	0.96	0.76-1.22	1.18	0.67-2.09
Korean	1.21*	1.01-1.44	0.97	0.57-1.63	1.11	0.92-1.34	0.97	0.56-1.66
Indian	1.05	0.90-1.21	1.07	0.71-1.61	0.99	0.85-1.16	1.08	0.71-1.62
Pakistani	1.90*	1.36-2.64	0.43	0.06-3.06	1.97*	1.40-2.77	0.45	0.06-3.21

Reference group is white Americans. Multivariable analyses were adjusted for age, sex, region of residence within the United States, education level, household net worth, diabetes mellitus, hypertension, hyperlipidemia, obesity, myocardial infarction, congestive heart failure, peripheral vascular disease, cerebrovascular accident, renal insufficiency, coagulopathy, blood-loss anemia, deficiency anemias, systemic hypotension, skin cancer, cataract, pseudophakia or aphakia, diabetic retinopathy, and open-angle glaucoma.

* $P < 0.05$.

only one previous study that evaluated rates of AMD among Asian Americans. In that analysis involving 727 participants, predominantly Chinese Americans in San Francisco, enrolled in the MESA study, the prevalence of nonexudative AMD was lower in Chinese Americans (3.6%) than in non-Hispanic white Americans (4.8%), although the odds of exudative AMD were higher in Chinese Americans than in white Americans.¹⁰ Several possible reasons may explain the differences in findings between MESA and our present study. First, the MESA analysis controlled for only age and sex, whereas the abundant information on patients in the i3 Data Mart database allowed us to control for many additional potential confounding factors. Second, MESA was a cross-sectional study whereas the present analysis was a longitudinal study, and during each visit to an eye care provider, patients could have received an AMD diagnosis. Third, the Asian Americans in our report were approximately 10 years younger, on average, than the participants in MESA. Finally, there were very few Asian Americans (seven total) in MESA who received a diagnosis of late AMD.

Comparison with Studies from China and Japan

An interesting finding from our analysis was the large difference in nonexudative AMD rates between Japanese and Chinese Americans. Although population-based studies have been conducted in China and Japan, comparing results from those studies with our findings is challenging because of the large variability in prevalence rates described in the literature (China, 5.5%–9.2%; Japan, 4.3%–10%) for early AMD.^{6–9} In the present study, the prevalence of nonexudative AMD was 6.5% for Chinese Americans and 4.36% for Japanese Americans, each of which falls within the range of estimates from studies conducted in the respective country. Similarly, our prevalence rates for exudative AMD were consistent with those of previous population-based studies conducted in these two Asian nations (Chinese Americans 0.52% in the present study vs. 0.4%–1.9% from studies conducted in China; 0.59% for Japanese Americans in the present study vs. 0.6%–0.9% from studies conducted in Japan).^{6–9} Our prevalence estimates are also similar to pooled prevalence estimates of early and late AMD from a meta-analysis by Kawasaki et al.¹⁶ In their study of

FIGURE 2. Survival plot of developing nonexudative AMD in different Asian ethnicities.

FIGURE 3. Survival plot of developing exudative AMD in different Asian ethnicities.

persons of different Asian ethnicities (including Chinese, Japanese, Malaysians, South Koreans, and Indians) aged 40 to 79 years, the pooled prevalence rate was 6.8% for nonexudative AMD and 0.56% for exudative AMD.

After adjustment for confounding factors, the risk for nonexudative AMD was notably different in Japanese Americans, who had a 29% decreased risk for nonexudative AMD, and Chinese Americans, who had a 63% increased risk for nonexudative AMD, than it was in white Americans. The differences in rates of AMD among Chinese and Japanese Americans that we have identified are likely multifactorial, including genetic and environmental factors. Previous studies have suggested that the reduced AMD rates observed in Japan may be attributable to the types of foods Japanese people consume.^{6,17} Foods that are high in omega-3 long-chain fatty acids, such as oily fish, which are common in Japanese cuisine, may decrease the risk for early and late stages of AMD.^{18–20} If additional studies confirm these findings and further research identifies the factors responsible for the reduced AMD rates in this group, they may lead to novel ways to slow down or prevent the development of AMD in persons of other races.

Comparison with Previous Study of Racial Differences in AMD

The findings of this study complement the results of another study we performed using the same health care claims database from which we compared rates of nonexudative and exudative AMD between persons of different races in the United States. In that analysis, we found that 60-year-old Asian Americans had a 28% increased risk for nonexudative AMD compared with similarly aged white Americans but that, by age 80, there were no statistically significant differences in risk for nonexudative AMD between the groups. In our paper looking at racial differences in rates of AMD, when analyzing the data using Cox regression modeling, we noticed that there were nonproportional hazards. To properly interpret the model, we modified the Cox model to estimate hazard ratios separately by age. In the present study, there was insufficient evidence for nonproportional hazards; therefore, we were able to use the regular Cox proportional hazards model to estimate hazard ratios for various Asian ethnicities compared with white Americans, which assumes that the hazard ratios were same across all ages. We suspect the reason the proportional hazards assumption was violated in our earlier study but not in the present analysis might have been the varying proportions of the different Asian American ethnicities in different age groups in the database. Table 4 shows the number of persons of Asian ethnicities stratified by age group. The table shows that the combined proportion of Chinese and Pakistani Americans (Asian ethnicities that were shown in our earlier analysis to have a significantly greater hazard for nonexudative AMD compared with white Americans) increased from 39% in the 40- to 50-year-old Asian American population to 42% in the 70- to 80-year-old Asian American population. However, the percentage of Japanese (the

Asian ethnicity that was shown to have a significantly reduced hazard for nonexudative AMD compared with white Americans) increased from 10% in the 40- to 50-year-old Asian American population to 21% in the 70- to 80-year-old Asian American population. Hence, the Asian ethnicities with increased hazards for nonexudative AMD were found to dominate the lower age groups much more than they were found to dominate the higher age groups. This change in the relative proportions of subgroups with opposing hazards for the outcome may explain why, in the present study, there were proportional hazards between different Asian ethnicities as age progressed, whereas there was evidence of nonproportional hazards in our earlier study, which treated all Asian Americans as one group and compared them with white Americans.

Study Strengths and Weaknesses

A benefit of using claims data to study the risk for AMD among persons of different Asian ethnicities is the large sample size and the adequate representation of those ethnicities. In this analysis, there were more than 1000 enrollees in seven Asian ethnicities. These large numbers allow for comparisons of differences in AMD risk among the subgroups. A similarly sized population-based study, using fundus photography, would cost millions of dollars and take many years to complete. In addition, unlike other studies that assess persons in a specific city or academic medical center or those willing to participate in a population-based study, this study was not confined to studying people in one particular community. Finally, by obtaining data from thousands of eye care providers across the country, our study may be a better reflection than previous studies of the actual burden of AMD throughout the entire US.

Several limitations must be acknowledged. First, some population-based studies report prevalence rates for “early” versus “late” AMD; however, because AMD in this analysis was diagnosed by billing codes, we could only classify it into nonexudative or exudative disease. Although many persons with early AMD have nonexudative AMD, those with late AMD often include patients with geographic atrophy and those with exudative disease. Also included in the category of exudative AMD is polypoidal choroidal vasculopathy (PCV), which has been found to be more common in Asians, and it has been suggested that this may explain why some studies have found Asian Americans to have higher rates of exudative AMD than white Americans.²⁰ Because PCV is often clinically indistinguishable from choroidal neovascularization and lacks its own diagnostic billing code, it is difficult to determine the extent to which this may be affecting the rates of exudative AMD we report. Second, our study included only patients insured through one specific managed care network. Additional studies are necessary to study rates of AMD in other groups, including uninsured or underinsured patients. Similarly, enrollees who have ocular comorbidities or ocular symptoms are more likely to seek eye care, which would increase their chances of getting diagnosed with conditions such as AMD. Although our multivariable mod-

TABLE 4. Age Distribution of the Asian American Ethnicities in the Plan

	Chinese	Pakistani	Japanese	Vietnamese	Filipino	Korean	Indian	Other Asian	Total
Age (y)	<i>n</i> (%)	<i>n</i> (%)	<i>n</i> (%)	<i>n</i> (%)	<i>n</i> (%)	<i>n</i> (%)	<i>n</i> (%)	<i>n</i> (%)	<i>N</i>
40–49	6,921 (36.3)	535 (2.8)	1,900 (10.0)	2,307 (12.1)	996 (5.2)	1,561 (8.2)	3,808 (20.0)	1,054 (5.5)	19,082
50–59	5,358 (35.3)	314 (2.1)	1,525 (10.0)	2,037 (13.4)	839 (5.5)	1,321 (8.7)	3,062 (20.1)	744 (4.9)	15,200
60–69	2,522 (35.5)	126 (1.8)	782 (11.0)	883 (12.4)	483 (6.8)	806 (11.3)	1,200 (16.9)	306 (4.3)	7,108
70–79	912 (40.9)	22 (1.0)	458 (20.5)	172 (7.7)	153 (6.9)	207 (9.3)	214 (9.6)	92 (4.1)	2,230
≥80	205 (42.4)	3 (0.6)	106 (22.0)	21 (4.4)	43 (8.9)	53 (11.0)	28 (5.8)	24 (5.0)	483
Total	15,918	1,000	4,771	5,420	2,514	3,948	8,312	2,220	44,103

els controlled for common ocular comorbidities, our incidence and prevalence estimates are not adjusted for these factors. This must be kept in mind when comparing our AMD incidence and prevalence estimates with those of population-based epidemiologic studies in the literature. Third, several important clinical factors, such as visual acuity, smoking history, and disease specifics, are not captured in the database and, therefore, could not be adjusted for in the models. Fourth, unlike many population-based studies that often have a retina specialist review fundus photographs to determine the presence of AMD, we captured care provided by all different types of eye care providers with varying levels of experience diagnosing this condition. Fifth, some of the enrollees in this analysis might not have undergone dilated funduscopy examination. Given that AMD is much easier to identify after dilation, we may be underestimating the true prevalence of these conditions compared with some other studies.

Implications

As a follow-up to a recent study we conducted that found 60-year-old Asian Americans had a 28% higher risk for AMD than similarly aged white Americans,⁵ in this analysis we were able to further explore the burden of AMD among Asian Americans based on ethnicity. When doing so, after adjustment for confounding factors, we identified significant differences in rates of nonexudative AMD among different Asian ethnicities. Chinese and Pakistani Americans experienced significantly higher risk for nonexudative AMD, whereas Japanese Americans had a 29% reduced risk for nonexudative AMD. Further research must be conducted to determine whether the differences in rates of nonexudative AMD between Asian ethnicities are attributable to genetic factors, environmental factors, or both.

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