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Prevalence of and Risk Factors for Age-Related Macular Degeneration in a Multiethnic Asian Cohort

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Objective: To describe the prevalence of and risk factors for age-related macular degeneration (AMD) in a multiethnic Asian cohort of Chinese, Malay, and Indian persons.

Methods: In this population-based study, 3172 persons of Chinese, Malay, and Indian ethnicities 40 years and older were included. Participants underwent comprehensive systemic and ocular examination, retinal photography, and laboratory investigations. Early and late AMD signs were graded from retinal photographs. Age-standardized prevalence estimates were calculated using the 2010 Singapore adult population as the standard population. Association with a range of systemic risk factors was analyzed.

Results: Of 3172 participants, AMD was present in 211 subjects. Age-standardized prevalence of AMD was 7.0%

in persons 40 years and older. The age-standardized prevalence was similar in all 3 Asian ethnic groups: Chinese, 7.3%; Malay, 7.7%; and Indian, 5.7% (P value = .44). The prevalence increased with age and was higher in men. Of the range of risk factors evaluated, only myopic refractive error (<-0.5 D) was significantly associated with a lower risk for AMD (odds ratio, 0.44; $P < .001$, compared with emmetropia) in Chinese men.

Conclusions: The prevalence of AMD was similar in the 3 major ethnic groups in Asia and comparable with white populations. Myopic refractive error was associated with reduced risk of AMD in Chinese men.

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AGE-RELATED MACULAR DEGENERATION (AMD) is one of the leading causes of blindness in the elderly population.¹⁻⁴ Despite its importance as an aging condition in Asia, there are few population-based studies conducted in Asian populations. Early clinical reports have suggested that AMD is less frequent in Asian individuals than in white individuals,⁵ but more recent population-based data from China,⁶ India,^{7,8} Japan,^{9,10} Taiwan,¹¹ and Malay individuals in Singapore¹² have allowed more precise estimates of the prevalence of AMD in Asian individuals. In a meta-analysis, it was suggested that AMD was as common in Asian populations as in white populations, with pooled prevalence estimates of 6.8% for early AMD and 0.56% for late AMD in Asian populations aged 40 to 79 years.¹³ However, even within Asia, there may be significant ethnic/racial differences, with some reports of AMD prevalence as low as 1.6% and 2.5% in Chinese individuals from the Beijing Eye Study⁶ and the Multi-ethnic

Study of Atherosclerosis,² respectively. Whether these variations are real or related to methodological differences in study design are unclear.

Among the identified risk factors, smoking is the most consistent risk factor, reported to increase the risk of neovascular AMD by up to 3 to 4 times.¹⁴⁻¹⁷ Associations have been less consistently seen for other risk factors, such as hypertension/blood pressure, diabetes mellitus, lipid level, cardiovascular disease, and inflammatory markers (eg, C-reactive protein level).¹⁴⁻¹⁷ Few have comprehensively examined these risk factors in different Asian populations.

There is evidence that a hyperopic refractive error may also be associated with an increased risk of AMD (and conversely a myopic refraction associated with a lower AMD risk), but results are not consistent.¹⁸⁻²⁵ Recently, our group reported an association between hyperopic refractive error and shorter axial length with higher risk of early AMD in a Malay population; for each diopter (D) increase in hyperopic refraction and each millimeter de-

crease in axial length, an 8% and 29% increased risk of early AMD was reported, respectively.²⁶ Nevertheless, studies of these associations in different Asian ethnic groups remain limited.

In the current study, we aimed to describe the prevalence and risk factors for AMD in a large multiethnic Asian cohort of Chinese, Malay, and Indian persons, representing the 3 major racial/ethnic groups in Asia.

METHODS

This study was performed in accordance with the tenets of the Declaration of Helsinki and approved by the local institutional review board at each site. Informed consent was obtained from each study subject.

STUDY POPULATION

The present study used data from the Singapore Prospective Study Program, which included participants from 4 previous cross-sectional studies: Thyroid and Heart Study 1982-1984,²⁷ 1992 Singapore National Health Survey,²⁸ National University of Singapore Heart Study 1993-1995,²⁹ and 1998 Singapore National Health Survey.³⁰ All studies involved a random sample of individuals from the Singapore population, aged 24 to 95 years, with disproportionate sampling stratified by ethnicity to ensure sufficient sample size in minority ethnic groups (Malay and Indian individuals). The study sample was selected by the Ministry of Health, Singapore.

From 2003 to 2007, 10 747 participants were invited to participate in the current study by linking their unique national identification numbers with national registries. After excluding participants with identification errors (n=85) and those who were deceased (n=592), left the country (n=6), were unable to be contacted after 3 different home visits (n=2292), and refused to participate (n=30), 7742 participants were interviewed at their homes and were then invited to a comprehensive clinic examination at the Singapore Eye Research Institute that included systemic and ocular examination, retinal photography, and laboratory investigations.^{31,32}

Of these 7742 participants, 5157 attended the clinical examination. Logistic constraints due to availability of only 1 retinal camera resulted in only 1 in 2 Chinese participants (the group with the largest sample size) able to have retinal photography between March 19, 2005, and February 20, 2006.^{31,32} As a result, retinal photography was offered to 4137 participants (80.2%) of those who attended the clinic. Of these, 4098 (99.2%) had retinal photographs of sufficient quality for grading of retinal signs. We further excluded participants whose retinal photographs were ungradable for AMD (n=220) and those who were younger than 40 years (n=706), leaving 3172 participants in the present analysis. Excluded participants tended to be older and have higher systolic blood pressure, lower low-density lipoprotein cholesterol level, and higher high-density lipoprotein cholesterol level (all $P < .05$) than included participants.

RETINAL PHOTOGRAPHY AND AMD GRADING

Photograph grading was performed in a standard manner according to the protocol used in the Multi-ethnic Study of Atherosclerosis.² Among the AMD features evaluated were drusen size, type, and area; increased retinal pigment; retinal pigment epithelial depigmentation; pure geographic atrophy; and signs of exudative macular degeneration. Drusen were classified as hard or soft; then soft drusen were divided into distinct and indistinct soft drusen. Early AMD was defined by either any

soft drusen (distinct or indistinct) and pigmentary abnormalities or large soft drusen 125 μm or more in diameter with a large drusen area ($>500\text{-}\mu\text{m}$ -diameter circle) or large soft indistinct drusen in the absence of signs of late AMD. Late AMD was defined by the presence of any of the following: geographic atrophy or pigment epithelial detachment, subretinal hemorrhage or visible subretinal new vessel, or subretinal fibrous scar or laser treatment scar for AMD.

RISK FACTORS

An interviewer-administered questionnaire was used to collect information on sociodemographic and lifestyle factors. Physical examination included anthropometric measurements, blood pressure, and detailed ocular examination including retinal photography. Laboratory examination included measurement of fasting plasma glucose, lipid, serum creatinine, and C-reactive protein levels.

Education was categorized into (1) primary or lower (≤ 6 years), (2) secondary (7-10 years), and (3) postsecondary (≥ 11 years, including university education). Cigarette smoking was categorized into current smokers and former or nonsmokers. Among the current smokers, the quantity of cigarettes smoked (sticks per day) was categorized into 2 groups, 20 or more sticks/d and less than 20 sticks/d. Alcohol consumption was categorized into drinkers (those who reported having drunk alcohol in the past 3 months, irrespective of quantity) and nondrinkers. Cardiovascular disease was defined as self-reported myocardial infarction or angina or stroke. The average of the 2 systolic and diastolic blood pressure measurements was used as the systolic and diastolic blood pressure value. Hypertension was defined as systolic blood pressure of 140 mm Hg or more or diastolic blood pressure of 90 mm Hg or more or self-reported physician-diagnosed hypertension. Diabetes mellitus was defined as a fasting plasma glucose level of 126 mg/dL or more or self-reported physician-diagnosed diabetes or use of glucose-lowering medication. Dyslipidemia was defined as a total cholesterol level of 239.4 mg/dL or more (to convert to millimoles per liter, multiply by 0.0259), low-density lipoprotein cholesterol level of 158.3 mg/dL or more (to convert to millimoles per liter, multiply by 0.0259), high-density lipoprotein cholesterol level of less than 38.6 mg/dL (to convert to millimoles per liter, multiply by 0.0259), or self-reported physician-diagnosed dyslipidemia. Chronic kidney disease was defined as an estimated glomerular filtration rate of less than 60 mL/min per 1.73 m².³²⁻³⁴ Ankle pressures were measured using a standardized Doppler ultrasonography device (8 MHz, Smart-Dop 20EX, bidirectional blood flow detector; Hadeco). Measurements were carried out after a 5-minute rest in the supine position. Ankle brachial index was calculated as the ratio of the higher of the 2 systolic pressures at the ankle to the average of the right and left brachial artery pressures, unless there was a discrepancy of 10 mm Hg or more in blood pressure values between the 2 arms. Peripheral artery disease was defined as an ankle brachial index of 0.9 or less in at least 1 leg.³⁵⁻³⁷

Objective refraction was measured using an autorefractor machine (Canon RK-5 Autorefractor Keratometer; Canon Inc Ltd). Spherical equivalent (SE) of each eye, measured in diopters, was calculated using the spherical dioptric power plus half the cylindrical dioptric power. Participants with aphakia or pseudophakia in one or both eyes (n=155) were excluded. Emmetropia was defined as SE between +0.5 D or less and -0.5 D or more. Mild myopia was defined as SE between less than -0.5 D and -5.0 D or more, and high myopia was defined as SE less than -5.0 D. Hyperopia was defined as SE of more than +0.5 D, with mild hyperopia defined as SE more than 0.50 D and less than +2.00 D and high hyperopia as SE of +2.00 D or more.

Table 1. Characteristics of the Participants of the Singapore Prospective Study Program by AMD Status

Characteristic	No. (%)			P Value ^a
	All (n=3172)	No AMD (n=2961)	Any AMD (n=211)	
Age, y, mean (SD)	53.73 (9.51)	53.48 (9.34)	57.28 (11.08)	<.001
Male	1561 (49.2)	1411 (47.7)	150 (71.1)	<.001
Race				
Chinese	1910 (60.2)	1784 (60.2)	126 (59.7)	.45
Malay	645 (20.3)	596 (20.1)	49 (23.2)	
Indian	617 (19.5)	581 (19.6)	36 (17.1)	
Total cholesterol level, mg/dL, mean (SD)	204.6 (36.7)	205.0 (36.3)	200.8 (40.2)	.11
LDL cholesterol level, mg/dL, mean (SD)	125.9 (32.8)	125.87 (32.8)	123.2 (35.1)	.26
HDL cholesterol level, mg/dL, mean (SD)	53.7 (13.1)	53.7 (13.1)	52.1 (12.4)	.09
BMI, mean (SD)	24.37 (4.32)	24.40 (4.34)	23.94 (4.10)	.13
Systolic BP, mm Hg, mean (SD)	135.40 (21.11)	135.03 (20.98)	140.32 (22.39)	<.001
Diastolic BP, mm Hg, mean (SD)	79.19 (10.79)	79.05 (10.74)	81.12 (11.36)	.007
Diabetes mellitus	413 (13.1)	380 (12.9)	33 (15.7)	.24
Hypertension	1500 (47.9)	1383 (47.3)	117 (56.0)	<.001
History of CVD	74 (2.3)	65 (2.2)	9 (4.3)	.06
Smoking status				
Never smoked	2507 (79.3)	2355 (79.8)	152 (72.0)	.03
Past smoker	283 (9.0)	257 (8.7)	26 (12.3)	
Current smoker	372 (11.8)	339 (11.5)	33 (15.6)	
Consumed alcohol within past 3 mo	663 (20.9)	622 (21.0)	41 (19.4)	.59
Low socioeconomic status	145 (4.4)	131 (4.4)	9 (4.3)	.92
Refractive error (n=3607)				
Myopia	1195 (40.6)	1142 (41.5)	53 (27.6)	.001
Emmetropia	794 (27.0)	732 (26.6)	62 (32.3)	
Hyperopia	952 (32.5)	875 (31.8)	77 (4.1)	

Abbreviations: AMD, age-related macular degeneration; BMI, body mass index (calculated as weight in kilograms divided by height in meters squared); BP, blood pressure; CVD, cardiovascular disease; HDL, high-density lipoprotein; LDL, low-density lipoprotein.
SI conversion factors: To convert HDL, LDL, and total cholesterol to millimoles per liter, multiply by 0.0259.

^aP value from a test for any differences between AMD status, adjusted for age in analysis of covariance models.

Table 2. Prevalence of Age-Related Macular Degeneration in Chinese, Malay, and Indian Participants Stratified by Age and Sex

Characteristic	All		Chinese		Malay		Indian	
	No. at Risk	No. (%)	No. at Risk	No. (%)	No. at Risk	No. (%)	No. at Risk	No. (%)
Age group, y								
40-49	1343	63 (4.7)	806	36 (4.5)	300	15 (5.0)	237	12 (5.1)
50-59	1106	69 (6.2)	655	43 (6.6)	213	17 (8.0)	238	9 (3.8)
60-69	473	40 (8.5)	313	25 (8.0)	83	8 (9.6)	77	7 (9.1)
70-79	233	38 (16.3)	127	21 (16.5)	43	9 (20.9)	63	8 (12.7)
≥80	17	1 (5.9)	9	1 (11.1)	6	0	2	0
Crude prevalence	3172	6.7%	1910	6.6%	645	7.6%	617	5.8%
Age-standardized prevalence, % (95% CI) ^a		7.0 (6.0-8.4)		7.3 (5.8-9.7)		7.7 (5.7-10.8)		5.7 (3.9-11.3)
Characteristic	Male (n=1561)	Female (n=1611)	Male (n=927)	Female (n=983)	Male (n=323)	Female (n=322)	Male (n=311)	Female (n=306)
Crude prevalence, %	9.6	3.8	9.7	3.7	11.5	3.7	7.4	4.2
Age-standardized prevalence, % (95% CI) ^a	9.7 (8.1-11.6)	4.0 (3.0-9.6)	10.1 (8.0-12.8)	3.6 (2.5-22.9)	11.5 (8.1-16.5)	4.0 (2.0-9.9)	7.0 (4.4-13.8)	4.5 (2.4-7.8)

Abbreviation: CI, confidence interval.

^aStandardized to 2010 Singapore population census.

STATISTICAL ANALYSIS

All statistical analyses were performed using SPSS version 16 (IBM SPSS). Characteristics of the study population were examined using proportions or means and standard deviation (**Table 1**). Age-standardized prevalence estimates were calculated by the direct method using the 2010 Singapore adult

population as the standard population (**Table 2**).³⁸ The age strata-specific prevalence rates were weighted by the proportions of the corresponding strata in the population census, then summed to give a summary prevalence rate. Because of the strong sex difference in the prevalence of AMD in this population, subsequent analyses were stratified by sex to look into risk factors separately. The relationship between any AMD (early or late

Table 3. Age- and Race-Adjusted OR of Age-Related Macular Degeneration

Characteristics	Men		Women	
	Age-Race-Adjusted OR (95% CI)	P Value	Age-Race-Adjusted OR (95% CI)	P Value
Age, y	1.04 (1.02-1.05)	<.001	1.03 (1.01-1.06)	.02
Race				
Chinese	1 [Reference]		1 [Reference]	
Malay	1.26 (0.84-1.90)	.27	1.03 (0.53-2.01)	.93
Indian	0.71 (0.44-1.15)	.17	1.15 (0.60-2.19)	.68
Total cholesterol level	0.89 (0.74-1.08)	.23	1.03 (0.79-1.34)	.85
LDL cholesterol level	0.89 (0.72-1.10)	.28	1.04 (0.77-1.39)	.80
HDL cholesterol level	0.83 (0.45-1.55)	.56	1.86 (0.89-3.87)	.10
Systolic BP	1.00 (0.99-1.01)	.50	1.00 (0.99-1.02)	.56
Diastolic BP	1.00 (0.99-1.02)	.84	1.01 (0.98-1.03)	.70
Diabetes mellitus	0.98 (0.60-1.59)	.93	1.04 (0.49-2.23)	.92
Hypertension	0.99 (0.68-1.44)	.96	1.08 (0.61-1.92)	.80
History of CVD	1.25 (0.47-2.74)	.58	1.54 (0.20-12.03)	.68
C-reactive protein	0.98 (0.95-1.02)	.40	0.99 (0.94-1.04)	.68
Peripheral artery disease	0.95 (0.43-2.08)	.89	1.10 (0.39-3.17)	.86
Chronic kidney disease	1.63 (0.98-2.71)	.06	0.76 (0.26-2.24)	.62
Low socioeconomic status	0.87 (0.41-2.13)	.87	0.53 (0.13-2.23)	.39
Consumed alcohol in past 3 mo	0.92 (0.61-1.39)	.70	0.40 (0.12-1.29)	.13
Smoking status				
Nonsmoker	1 [Reference]		1 [Reference]	
Past smoker	0.89 (0.55-1.43)	.62	3.29 (0.73-14.87)	.12
Current smoker	1.02 (0.66-1.56)	.94
Smoking status (1)				
Nonsmoker/past smoker	1 [Reference]		1 [Reference]	
Current smoker: ≥20 sticks/d	1.24 (0.67-2.30)	.49
Current smoker: <20 sticks/d	0.82 (0.47-1.43)	.49
Smoking status (2)				
Nonsmoker	1 [Reference]		1 [Reference]	
Past/current smoker	0.96 (0.67-1.36)	.81	1.23 (0.29-5.24)	.78
Refractive error				
Emmetropia	1 [Reference]		1 [Reference]	
Hyperopia	0.73 (0.47-1.12)	.15	1.72 (0.85-3.48)	.13
Myopia	0.44 (0.28-0.70)	<.001	0.96 (0.45-2.04)	.91

Abbreviations: BP, blood pressure; CI, confidence interval; CVD, cardiovascular disease; HDL, high-density lipoprotein; LDL, low-density lipoprotein; OR, odds ratio.

AMD) and risk factors was analyzed using logistic regression adjusting for age and race. Potential confounders ($P < .30$) in **Table 3** were considered for multivariable analysis in **Table 4**. Stepwise selection was used to select the final covariates for adjustment, which included age, race, smoking status, chronic kidney disease, and refractive error. Statistical analysis was performed using the statistical software SPSS version 13 (IBM SPSS). $P < .05$ indicated statistical significance.

RESULTS

In total, 3172 participants 40 years and older with sufficient-quality photographs to grade AMD signs were included. The characteristics of participants and risk factors have been summarized in Table 1. The mean (SD) age of participants was 53.73 (9.51) years (range, 40-95 years) and 1561 (49.2%) were men. The study population consisted of 1910 Chinese (60.2%), 645 Malay (20.3%), and 617 Indian (19.5%) individuals. Myopia was the most common refractive error (40.6%), followed by hyperopia (32.5%) and emmetropia (27.0%).

Any AMD was present in 211 subjects, early AMD in 203 subjects, and late AMD in 8 subjects. The crude and age-standardized prevalences of AMD according to race

and sex are summarized in Table 2. Crude prevalence was 6.7% and age-standardized prevalence was 7.0% among persons 40 years and older. Age-standardized prevalence of AMD was similar in the 3 racial groups (Chinese, 7.3%; Malay, 7.7%; and Indian, 5.7%; P value = .44). The prevalence of AMD increased from 4.7% in subjects aged 40 to 49 years to 16.3% in subjects aged 70 to 79 years. This increasing prevalence with age was observed in all 3 racial groups. Age-related macular degeneration was significantly more prevalent in men in all 3 ethnic groups.

Analysis of the relationship between any AMD and risk factors stratified by sex is summarized in Table 3. After adjusting for age and race, myopia was significantly associated with reduced risk of any AMD (odds ratio, 0.44; $P < .001$) in male participants. There was no significant association between AMD and dyslipidemia, hypertension, C-reactive protein level, peripheral artery disease, chronic kidney disease, socioeconomic status, and smoking status.

The multivariate-adjusted odds ratios for association between AMD and risk factors studied are summarized in Table 4. In male participants, myopia was signifi-

Table 4. Multivariate-Adjusted ORs for Age-Related Macular Degeneration

Characteristics	All		Chinese		Malay		Indian	
	Multivariate-Adjusted OR (95% CI) ^a	P Value	Multivariate-Adjusted OR (95% CI) ^a	P Value	Multivariate-Adjusted OR (95% CI) ^a	P Value	Multivariate-Adjusted OR (95% CI) ^a	P Value
Men								
Age, y	1.03 (1.01-1.05)	.002	1.03 (1.00-1.05)	.02	1.03 (0.99-1.07)	.11	1.03 (0.99-1.08)	.19
Race								
Chinese	1 [Reference]		
Malay	1.28 (0.83-1.96)	.27	
Indian	0.65 (0.38-1.09)	.10	
Chronic kidney disease	1.48 (0.85-2.57)	.17	1.49 (0.70-3.14)	.30	2.44 (0.98-6.10)	.06
Smoking status								
Nonsmoker	1 [Reference]		1 [Reference]		1 [Reference]		1 [Reference]	
Past smoker	0.86 (0.51-1.44)	.56	1.10 (0.57-2.11)	.78	0.61 (0.21-1.74)	.35	0.66 (0.14-3.13)	.60
Current smoker	1.03 (0.66-1.61)	.91	0.96 (0.51-1.81)	.91	1.06 (0.48-2.35)	.89	1.11 (0.37-3.36)	.86
Refractive error								
Emmetropia	1 [Reference]		1 [Reference]		1 [Reference]		1 [Reference]	
Hyperopia	0.75 (0.49-1.16)	.20	0.70 (0.40-1.26)	.24	0.88 (0.37-2.09)	.77	0.81 (0.27-2.39)	.70
Myopia	0.45 (0.28-0.70)	.001	0.40 (0.23-0.72)	.002	0.50 (0.20-1.29)	.15	0.50 (0.14-1.80)	.29
Women								
Age, y	1.02 (0.99-1.05)	.23	1.00 (0.96-1.05)	.85	1.03 (0.96-1.10)	.43	1.05 (0.98-1.11)	.16
Race								
Chinese	1 [Reference]		
Malay	1.17 (0.59-2.33)	.65	
Indian	1.32 (0.64-2.71)	.46	
HDL cholesterol level	1.90 (0.89-4.03)	.10	1.97 (0.78-4.98)	.15	3.03 (0.49-18.8)	.23	0.70 (0.07-6.75)	.76
Smoking status								
Nonsmoker	1 [Reference]		1 [Reference]		1 [Reference]		1 [Reference]	
Past/current smoker	1.41 (0.33-6.06)	.65	0.90 (0.12-6.84)	.92	7.45 (0.72-77.0)	.09
Refractive error								
Emmetropia	1 [Reference]		1 [Reference]		1 [Reference]		1 [Reference]	
Hyperopia	1.70 (0.84-3.46)	.14	1.49 (0.57-3.91)	.42	3.59 (0.68-18.8)	.13	1.42 (0.35-5.83)	.63
Myopia ^b	0.95 (0.45-2.02)	.90	1.01 (0.40-2.58)	.98	0.70 (0.09-5.29)	.73	0.84 (0.14-5.23)	.85

Abbreviations: CI, confidence interval; D, diopter; HDL, high-density lipoprotein; OR, odds ratio; SE, spherical equivalent.

^aIn men, adjusted for age, race, chronic kidney disease, smoking status, and refractive error. In women, adjusted for age, race, HDL cholesterol level, smoking status, and refractive error.

^bMyopia: SE less than -0.50 D; emmetropia: SE -0.50 D or more to +0.50 D or less; and hyperopia: SE more than 0.50 D.

cantly associated with reduced risk of any AMD (odds ratio, 0.45; $P = .001$) compared with emmetropia as a reference, after adjusting for age, race, chronic kidney disease, and smoking status. Further analysis stratified by race showed that the reduced risk of AMD in myopia was only seen in Chinese men (odds ratio, 0.40; $P = .002$), but not in Malay and Indian men or female participants.

COMMENT

To our knowledge, this is the first population-based study to document the prevalence and risk factors for AMD in a multiethnic Asian cohort of Chinese, Malay, and Indian persons, representative of the 3 major racial/ethnic groups comprising nearly 3 billion people in Asia. The age-standardized prevalence of any AMD among persons 40 years and older was 7.0%. These figures are similar to results from a recent meta-analysis of Asian and white persons by Kawasaki and colleagues,¹³ who reported an age-standardized pooled prevalence of 6.8% for early AMD and 0.56% for late AMD in Asian individuals. These were not significantly different from the prevalence in mainly white populations of 8.8% for early AMD and 0.56% for late AMD ($P = .43$).¹³ Our study now

provides important confirmatory evidence using a single-study method that AMD is as common in different Asian ethnic groups as in white populations.

Importantly, we also demonstrate that there was no significant difference in age-standardized prevalence of AMD between the 3 Asian ethnic groups studied. The prevalence of AMD from the Malay group in the current study (7.7%) is slightly higher than that reported previously in the Singapore Malay Eye Study, which reported an age-standardized prevalence of 5.2% for early AMD in persons aged 40 to 80 years.^{12,17}

Previous studies from Asian populations⁹⁻¹² have reported higher AMD prevalence among men. This has been speculated to be partly related to a higher smoking rate in Asian men than women and partly due to the male dominance in polypoidal choroidal vasculopathy in Asian men.^{13,39} Our results also indicated a higher prevalence of AMD among men. However, this was not related to a higher prevalence of smoking in men, because we did not find a relationship between smoking and AMD.

Myopia was significantly associated with a reduced risk of any AMD in the current study. The apparent protective effect of myopia was only significant in Chinese men, although the pattern and direction of associations was simi-

lar in Malay men and Indian men. The larger number of Chinese subjects (60.2% of the study population) and a higher percentage with myopic refractive error in Chinese individuals might have explained the more apparent association than in Malay and Indian individuals.

So far, results from several other population-based and case-control reports have shown an inconsistent and inconclusive association between refractive errors and AMD. The Rotterdam Study,²³ the Age-Related Eye Disease Study,¹⁹ the Blue Mountains Eye Study,^{21,22} and the Beijing Eye Study⁴⁰ found an association between hyperopia and AMD, whereas the Beaver Dam Eye Study did not detect a correlation between both parameters, in both the 5-year²⁴ and 10-year AMD incidence reports.²⁵ The Blue Mountains Eye Study described a statistically weak association between AMD and hyperopia in a first report in 1998.²¹ However, the second report on the 5-year incidence of AMD did not support the previous observations.²² Suggested hypotheses for an increased risk of AMD in hyperopic subjects include common genetic risk, and increased sclera rigidity in hyperopic eyes may result in impaired transfer of oxygen and nutrients, thereby explaining the association with early AMD.^{41,42} The results from the current study are different and suggest myopia is negatively associated with AMD, while hyperopia did not confer any increased risk. A potential explanation is that myopia is often associated with higher education and socioeconomic status and therefore may appear to have a protective effect against AMD. A further potential confounder is the presence of nuclear cataract, which may result in myopic shift and protection against AMD.^{41,43} Sunlight exposure has been linked to increased risk of AMD.⁴⁴ The use of prescription spectacles in myopic subjects, providing protection against UV at the same time, might have contributed toward the apparent protective effect of myopia. The Beijing Eye Study, which studied 8655 eyes of 4376 Chinese subjects, reported that hyperopic refractive error ($P = .008$; 95% confidence interval, 1.04-1.28) was significantly associated with early AMD in Chinese adults.⁶ In a second report on the characteristics of 65 highly myopic eyes (myopia > -8 D),⁴³ highly myopic eyes were found to have significantly lower prevalence of early ($P = .03$; odds ratio, 3.0; 95% confidence interval, 1.21-7.51) and late ($P = .001$; odds ratio, 6.33) AMD than the non-highly myopic eyes. Highly myopic eyes were also associated with a lower number and smaller and less advanced type of macular drusen. A recent report of lower levels of vascular endothelial growth factor in myopic eyes suggested this may partly explain the apparent protective effect of myopia against AMD.⁴⁵

Of the range of major systemic risk factors examined, including smoking status, blood pressure, diabetes, dyslipidemia, peripheral artery disease, chronic kidney disease, and C-reactive protein level, no associations were found after age, sex, and race adjustment. Similarly, our previous study in a Singaporean Malay population has shown no associations between C-reactive protein level and AMD.⁴⁶ While smoking has been one of the most consistent associations with AMD,¹⁴⁻¹⁷ it is somewhat surprising that our current study did not demonstrate any association between current or past smoking with AMD compared with persons who never smoked.

Because of limitations in data gathering, we were unable to analyze further association between AMD and the smoking duration and pack-year variable. However, previous studies have found the link with smoking was strongest with late AMD.^{14,16,40} The small number of subjects with late AMD in the current study may explain the lack of association in this population. The number of past and current smokers was also smaller in our current population (20%) compared with 39% to 67.4% in previous studies that reported increased risk for AMD.^{12,16,17} Furthermore, previous studies in an Asian population, namely the Hisayama Study¹⁰ and the Beijing Eye Study,⁴⁰ also did not find an association between smoking and AMD. The inconsistency between these reports suggests that the impact of smoking on Asian AMD remains to be determined. Interestingly, different effects of smoking among ethnic groups have also been noted in coronary heart disease. The Chinese Multi-provincial Cohort Study reported smoking was associated with a lower relative risk of coronary heart disease among Chinese individuals.⁴⁷

The strengths of this study are the ability to study concurrently the 3 major ethnic groups in Asia and the standardized protocol used, including the photographic documentation of the macula. The large number of myopic participants allowed us to test the possible association between refractive error and AMD in a population with different refractive status compared with existing published studies. The limitations include the significant number of subjects who declined to join the present study. Excluded participants tended to be older compared with the participants and could have introduced bias in the subsequent prevalence estimation as well as low rates of late AMD. The long gap between invitation to the current study (2003-2007) and recruitment into the original studies (1982-1998) is likely to be an important factor. There were few cases of late AMD; therefore, we could not analyze the prevalence and risk factors for late AMD separately. The current study did not collect data on axial length. Finally, being a cross-sectional study, we cannot answer temporal questions that a longitudinal study could.

In conclusion, we report the prevalence of AMD in the 3 major ethnic groups in Asia, comprising Chinese, Malay, and Indian persons. We show the prevalence of AMD is comparable with white populations and is largely similar between the 3 Asian groups. Of the range of risk factors studied, myopic refractive error was associated with reduced risk of AMD in Chinese men.

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