PCV is a subtype of AMD or a different clinical entity remains controversial.

In this study, we performed a systematic review and meta-analysis aiming to summarize the prevalence of AMD in Asian studies and to investigate racial/ethnic differences with reported prevalence in white populations.

Methods

Sources and Methods of Literature Search

We assessed publications that reported prevalence or incidence of AMD among Asian populations. We searched the electronic databases of PubMed, Web of Science and EMBASE for relevant papers published from January 1996 through June 1, 2009, with the following search terms (formatted for PubMed search):

1. ("Macular Degeneration"[Mesh] AND ("Prevalence"[Mesh] OR "Epidemiology"[Mesh] OR "Cross-Sectional Studies"[Mesh] OR "Cohort Studies"[Mesh]))
2. (("age-related maculopathy"[All Fields] OR "age related maculopathy"[All Fields] OR "age-related macular degeneration"[All Fields] OR "age related macular degeneration"[All Fields] OR "macular degeneration"[All Fields]) AND ("prevalence"[All Fields] OR "incidence"[All Fields] OR "epidemiology"[All Fields] OR "risk factors"[All Fields]))
3. "Asia"[Mesh] OR "Asia"[All Fields] OR "Asian"[All Fields]
4. (#1 OR #2) AND #3

We searched for relevant studies from reference lists and review papers, and also asked local researchers to identify literature in the Japanese, Chinese, Indian, and Korean languages.

Study Selection

The 2 criteria for inclusion were (1) population-based study sample and (2) standardized assessment of AMD. We assessed the study reports from the literature to decide whether particular studies were population based (with a clear sampling frame derived from the community) and had used standardized grading methods to diagnose and classify AMD lesions (i.e., grading of retinal photographs following either the Wisconsin Age-Related Maculopathy Grading System [WARMGS][30] or the international classification proposed by the International ARM Epidemiological Study Group.[31]) with reproducible grading results. We excluded studies that only used a clinical examination by ophthalmoloscopy or slit-lamp biomicroscopic examination, because of the lack of any grading reproducibility assessment.

Quality Assessment

The quality of all selected articles was assessed by 1 of the investigators (RK) for the following attributes suggested by de Weerd et al:[32] (1) representative of the general older population and (2) appropriate recruitment of target population with response rate >50%. In brief, methods of sampling (e.g., population registries, inhabitants of defined areas, and patients registered with a general practice) were evaluated and recruitment of the study samples was considered appropriate if participants were recruited either randomly or from a defined geographic area.

Study Selection

Figure 1 shows the flow chart of the selection process used to identify relevant studies. We identified 9 relevant studies from 4 Asian countries/regions/ethnic groups (Japan, China, India, and Singapore) that met our criteria for inclusion in the review (Table 1). The prevalence data for AMD from mainly white populations were also reviewed for comparison with data from Asian populations and summarized using similar criteria. For studies conducted in mainly white populations, we included studies reporting age-gender specific prevalence that included ≥1000 study subjects.

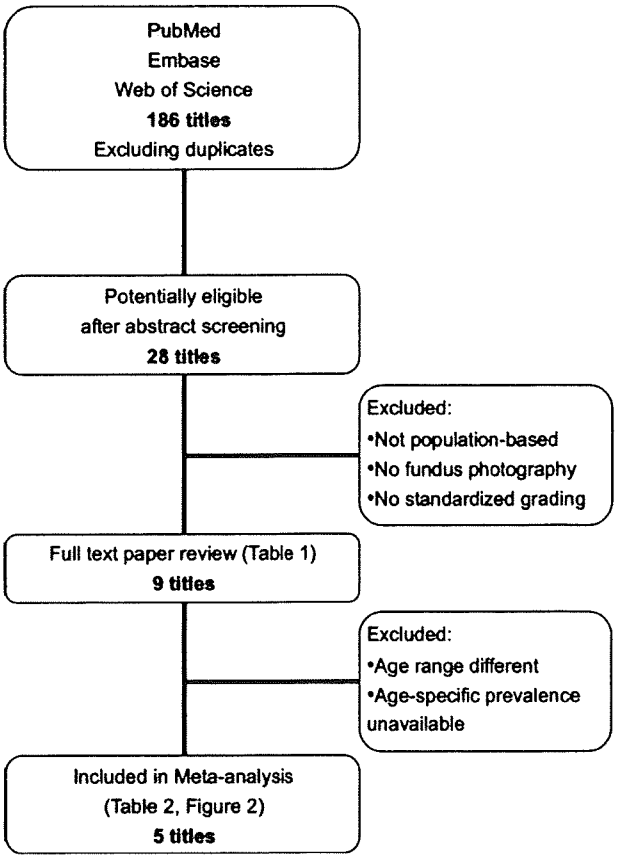

Figure 1. Results of literature search strategy.

Data Analysis

Age-specific pooled prevalence estimates of early and late AMD by the 40- to 49-, 50- to 59-, 60- to 69-, 70- to 79-, and ≥80-year-old age groups were calculated, using a random effect model with inverse-variance weighting. We allowed ≥5 years in age ranges for each age category (e.g., the reported prevalence for ages 43–54 years was pooled for the "40–49 years" age category).

Age-standardized prevalence rates with accompanying 95% confidence intervals (CI) across studies were estimated after direct age standardization to the world population aged 40 to 79 years, as reported by the World Health Organization[33] and pooled prevalence estimates determined. We limited this review to inclusion only of the age range 40 to 79 years as data for highest age category (≥80 years) varied widely across studies owing to relatively small numbers.

A test for heterogeneity (I-squared index) was performed to determine whether the differences in prevalence estimates across studies were greater than those expected by chance. A meta-regression model was built with ethnicity (Asian or white population) as the dependent variable to test the hypothesis that differ-

Table 1. Reported Prevalence of Age-related Macular Degeneration (AMD) in Asian Populations/Countries

Study	Year Examined	Age Range (yrs)	N	Response (%)	Photography	Grading System	Total (%)	Men (%)	Women (%)	Total (%)	Men (%)	Women (%)
Andhra Pradesh Eye Disease Study (India)[14,15]	1996–2000	≥40	3723	85%	30°, S, F	I	8.9	9.3	8.4	1.8	1.8	2.0
Hisayama Study (Japan)[10]	1998	≥50	1486	60.8%	45°, NS, F	I	12.7	13.9	11.9	0.9	1.7	0.3
Shihpai Eye Study (Taiwan)[13]	1999–2000	≥65	1361	54%	35°, NS, F	W	9.2	8.9	9.5	1.9	2.4	1.0
Funagata Study (Japan)[12]	2000–2002	≥35	1625	53.3%	45°, NS, F	W	3.5*	3.5*	3.5*	0.5*	0.8*	0.2*
Beijing Eye Study (China)[16,35]	2001	≥40	4439	83.4%	45°, NS, F	W	5.1	—	—	0.3	—	—
India Eye Study (India)[17]	2002–2003	50–79	1443	87%	35°, S, D	W	5.7	6.8	4.7	1.4	1.9	0.9
Japanese in Brazil[34]	2002–2003	≥60	478	80.5%	50°, NS, D	I	13.4	14.7	12.6	1.3	1.1	1.3
MESA (Chinese American, USA)[4]	2002–2004	45–85	699	70%	45°, NS, D	W	3.6	4.4	2.9	1.0	1.4	0.6
SiMES (Singapore)[11]	2004–2006	40–79	3265	78.7%	45°, NS, D	W	3.5	3.9	3.0	0.34	0.5	0.2

D = digital; F = 35-mm film; I = international classification proposed by the International ARM Epidemiological Study Group; MESA = Multi-Ethnic Study of Atherosclerosis; NR = not reported; NS = nonstereo; S = stereo; SD = standard deviation; SiMES = Singapore Malay Eye Study; W = Wisconsin Age-related Maculopathy Grading System or its modified system.
*Right eyes only.

ences existed in the AMD prevalence between the 2 ethnicities. Publication bias was assessed in a funnel plot with AMD prevalence estimates plotted against the standard error of prevalence estimates, using the Egger's test.

Results

The reported prevalence rates for early and late AMD are summarized in Table 1, grouped by the following ethnicities.

Japanese

There were 3 population-based studies in Japanese, which all enrolled participants from a defined geographic area with response rates between 53.3% and 80.5%.

The Hisayama Study (Japan, 1998).[10] In 1998, 1486 persons aged ≥50 years (60.8% response) in Hisayama, Japan, were examined for early and late AMD, the signs of which were defined following the International ARM classification. Prevalence of early and late AMD were 12.7% and 0.87%, respectively, and men had a higher prevalence of both AMD stages than women.

The Funagata Study (Japan, 2000–2002).[12] In 2000 to 20002, 1758 Japanese persons aged ≥35 years (53.3% response) in Funagata, Japan, were examined for AMD; 1625 participants (92.4%) had sufficient quality photographs for grading, which used the WARMGS. One limitation of this study was that only 1 eye per subject was photographed. In men, the age-standardized prevalence of late AMD was comparable between this study and the Blue Mountains Eye Study.

Japanese Immigrants and Their Descendants in Londrina, Brazil (2002–2003).[34] In 2002 to 2003, 483 Japanese immigrants and their descendants aged ≥60 years (80.5% response) were examined for AMD, the lesions of which were defined following the International ARM classification. Prevalence rates for early and late AMD were 13.4% and 1.3%, respectively. One in 4 (25%) patients with late AMD had PCV lesions.

Chinese

The Shihpai Eye Study (1999–2000).[13] From 1999 to 2000, 1105 persons aged ≥65 years (54% response) in Shihpai, Taiwan, were examined for AMD using the WARMGS. Overall prevalence rates for early and late AMD were 9.2% and 1.9%, respectively. Of 19 persons with late AMD, 2 (10.5%) were suspected to have PCV lesions defined by the typical orange colored polyp appearance.

The Beijing Eye Study (2001).[16,35] In 2001, 4376 Chinese persons aged ≥40 years (83.4% response rate) living in rural or urban regions of Beijing were assessed for AMD using the WARMGS. Prevalence rates for early and late AMD were 5.1% and 0.3%, respectively.

The Multi-ethnic Study of Atherosclerosis (2002–2004).[4] From 2000 to 2002, the Multi-ethnic Study of Atherosclerosis study examined 6176 subjects aged 45 to 84 years (70% response), including 727 Chinese Americans who were mainly born outside the United States. Signs of AMD were graded following a modification of the WARMGS. Late AMD was more prevalent in Chinese (1.0%) than in whites (0.6%).

Malays

The Singapore Malay Eye Study (2004–2006).[11] From 2004 to 2006, 3280 participants (78.7% response) in the Singapore Malay Eye Study were assessed for AMD using the WARMGS. This group represented an age-stratified random sample of Malay persons aged 40 to 80 years living in Singapore. Late (1.0% vs. 0.4%) and early AMD (6.1% vs. 3.8%) were more prevalent in men than women, although the gender difference in the prevalence of late AMD was not significant after adjusting for age and smoking (men compared with women; odds ratio, 1.39; 95% CI, 0.52–3.68 for late AMD; and odds ratio, 1.56; 95% CI, 1.11–2.20 for early AMD). This gender difference was not completely explained by the associated higher smoking rates in men.

Indians

The Andhra Pradesh Eye Disease Study (1996–2000).[14,15] A random sample of 3723 persons aged ≥40 years (85% response rate) from 94 clusters in 1 urban and 3 rural areas in Andhra Pradesh, India, were assessed from 1996 to 2000. Prevalence rates for early and late AMD were 8.9% and 1.8%, respectively. The age-specific prevalence of late AMD rose from 0.9% in persons aged 40 to 49 years to 3.7% in persons aged ≥70 years.

The India Eye Study (2002–2003).[17] From 2002 to 2003, 1443 persons aged ≥50 years (87% response rate) from a rural Indian population in 11 randomly sampled villages in Haryana, Northern India, were assessed for AMD signs using the WARMGS, with a late AMD prevalence of 1.4% (95% CI, 0.8%–2.3%).

South Koreans

There were 2 reports from South Korea describing AMD "prevalence" among healthy persons who participated in compulsory health screenings. Although these 2 studies had a large number of participants, they are likely to represent selective samples from the general population with an unknown denominator of the sampling frame or the total population of potential participants, and likely direction of any potential selection bias (i.e., whether participants were healthier or sicker than nonparticipants). For these 2 reasons, we have not included these 2 studies in further meta-analysis, but they are described below.

Kangbuk Samsung Hospital Study.[36] A total of 10 890 participants aged 50 to 92 years were assessed for AMD during calendar 2006, from fundus photographs grading using the International ARM classification. Age- and gender-adjusted prevalence rates for early and late AMD were 5.1% and 0.34%, respectively. Of the 9 patients with exudative AMD, 6 eyes (66.7%) had typical choroidal neovascularization, 2 (22.2%) had PCV, and 1 (11.1%) had retinal angiomatous proliferation, all confirmed by fluorescein angiography and indocyanine green angiography.

The Yonsei Medical Examination Center Study.[37] In 2006, 9468 participants of a health check who were aged ≥40 years at the Yonsei hospital were assessed for AMD, graded using the WARMGS. The results were categorized into the 4 stages proposed by the Rotterdam Eye Study.[38] There were 215 (2.3%) cases of early AMD and 20 (0.2%) cases of late AMD.

Pooled Prevalence Estimates of Early and Late Age-related Macular Degeneration in Asians

Age-specific pooled prevalence estimates of early and late AMD are shown in Figure 2. For early AMD, the pooled prevalence estimate and 95% CI for each age group was generally lower in

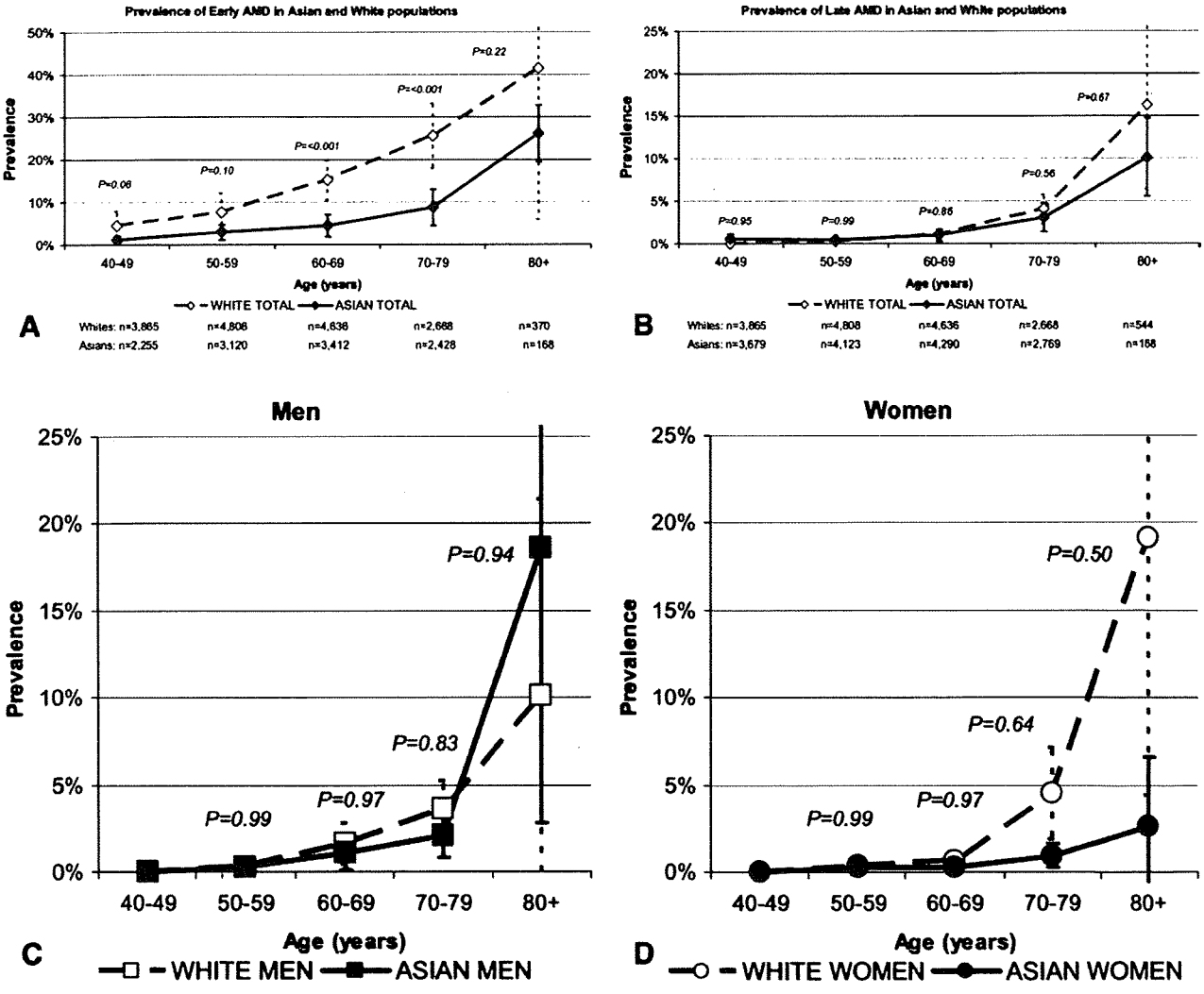

Figure 2. A, Age-specific pooled prevalence estimates of early AMD in Asian and white populations. B, Age-specific pooled prevalence estimates of late AMD in Asian and white populations. C, Age-specific pooled prevalence estimates of late AMD in Asian and white men. D, Age-specific pooled prevalence estimates of late AMD in Asian and white women. *P-value for comparison between Asian and white population. AMD = age-related macular degeneration.

Table 2. Comparison of Estimated Age-related Macular Degeneration (AMD) Prevalence in Populations Aged 40–79 Years

Study	N	Age-Standardized to the WHO World Population[33] aged 40–79 Years	
		Early AMD (%)	*Late AMD (%)*
Asian population			
Singapore Malay Eye Study[11]	3265	5.3 (4.4–6.1)	0.69 (0.40–0.98)
Hisayama study[10]	1486	10.9 (9.2–12.6)	0.72 (0.27–1.17)
Beijing Eye study[16,35]	4376	—	0.27 (0.04–0.41)
MESA (Chinese American)[4]	691	2.5 (2.0–2.9)	0.55 (0.37–0.73)
The India Eye Study[17]	1101	—	0.76 (0.38–0.13)
Pooled prevalence	10 919	6.8 (4.6–8.9)	0.56 (0.30–0.81)
Mainly White population			
Beaver Dam Eye Study[9]	4771	13.2 (12.2–14.2)	0.90 (0.68–1.11)
Blue Mountains Eye Study[40]	3428	3.9 (3.3–4.6)	0.55 (0.38–0.71)
Reykjavik Eye study[41]	1006	14.8 (13.3–16.4)	0.70 (0.36–1.00)
MESA (whites)[4]	2315	3.5 (2.9–4.1)	0.26 (0.15–0.37)
Baltimore Eye Study[3]	2418	—	0.64 (0.37–0.91)
Pooled prevalence	13 938	8.8 (3.8–13.8)	0.59 (0.35–0.84)

MESA = Multi-Ethnic Study of Atherosclerosis; WHO = World Health Organization.

Asians than that in whites, and the difference was significant for persons aged 60 to 79 years ($P<0.001$), but not for those <60 or ≥80 years (Fig 2*A*) For late AMD, the prevalence estimates and 95% CI among persons aged 40 to 79 years was similar between Asian and white populations (Fig 2*B*). Although the pooled prevalence of early and late AMD in persons aged ≥80 years were both higher in white populations (41.4% and 16.3%) than in Asian populations (26.1% and 10.1%), the 95% CI for both populations overlapped, so that these difference were not statistically significant (Fig 2*B*).

Pooled prevalence estimates for early and late AMD in Asian populations aged 40 to 79 years overall were 6.8% (95% CI, 4.6%–8.9%) and 0.56% (95% CI, 0.30%–0.81%), respectively (Table 2). The pooled prevalence of early and late AMD for the same age range in mainly white populations was slightly higher (8.8% [95% CI, 3.8%–13.8%] and 0.59% [95% CI, 0.35%–0.84%], respectively). However, there were no significant differences between Asian and white populations in the pooled prevalence of both early and late AMD in persons aged 40 to 79 years on meta-regression analysis ($P = 0.43$).

When stratified by gender, Asian men had higher point estimate of late AMD prevalence (18.6%) compared with white men (10.1%), whereas Asian women had lower point estimate prevalence (2.6%) than white women (19.1%; Fig 2*C, D*). However, the 95% CI for these point estimates overlapped between the 2 ethnicities, and were not statistically significantly different. A funnel plot (data not shown) demonstrated that there was no asymmetry for studies of AMD in Asian populations (Egger's test $P = 0.077$).

Summary of Evidence

In this systematic review and meta-analysis, we report that the prevalence of late AMD in persons aged 40 to 79 years was comparable between Asian and white populations. For early AMD, age-specific pooled prevalence estimates (Fig 2*A*) suggest that Asians have slightly lower prevalence than white persons (A, II). For persons aged ≥80 years, we could not conclude that there were differences in the prevalence of AMD between Asian and white populations because of the relatively small numbers in this older age group with limited available data. Because the prevalence of AMD in this oldest age category seems to be the main source of variation, this warrants further epidemiologic research targeting populations in the oldest age groups.

Discussion

Recent studies in Asian populations have reported higher late AMD prevalence among men compared with women.[10–13] Reasons for this disparity are speculated to be the substantially and uniformly higher smoking rate in Asian men than women,[12] together with the male dominance in prevalence of PCV lesions[19] that were not differentiated from typical neovascular AMD. We demonstrate that Asian men have higher late AMD prevalence compared with white men (Fig 2*C*). In contrast, Asian women had lower prevalence of late AMD compared with white women (Fig 2*D*).

In hospital-based studies in Asia, PCV is now recognized as being more common among patients with exudative AMD signs.[18,19,39] The frequency of PCV lesions among patients with exudative AMD in the Shihpai Eye Study,[13] the Kangbuk Samsung Hospital Study,[36] and study for Japanese immigrants in Brazil were 11%, 22%, and 25%, respectively. Although we were not able to have age-standardized comparisons of late AMD subtypes, the ratios of "neovascular AMD" to "geographic atrophy" shown in this report seem to be higher in Asian than white populations (Fig 3). The dominance of neovascular AMD cases over geographic atrophy cases in Asians is consistent with a higher frequency of PCV cases in Asians with neovascular AMD. However, the relatively high ratio of neovascular AMD to geographic atrophy could have resulted from either more neovascular AMD (PCV) cases or less geographic atrophy, or both, in Asians compared with whites. Interestingly, a higher frequency of neovascular AMD compared with geographic atrophy has also been reported in black

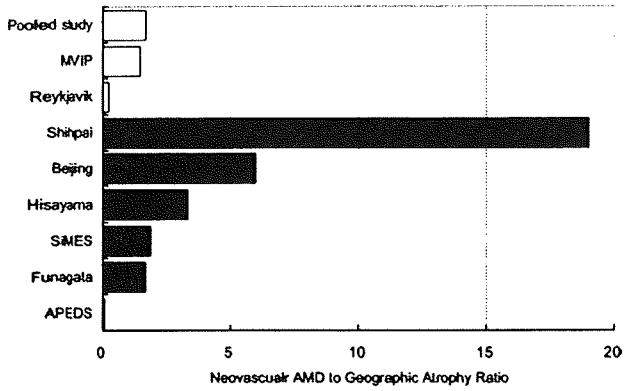

Figure 3. Ratios of 'Neovascular AMD to Geographic atrophy' in Asians (bars in black) and whites (bars in white). AMD = age-related macular degeneration; APEDS = Andhra Pradesh Eye Disease Study[32]; Beijing = Beijing Eye Study[29]; Funagata = Funagata Study[26]; Hisayama = Hisyama Study[25]; MVIP = Melbourne Vision Impairment Project[40]; Pooled study = Pooled study of the Beaver Dam Eye Study, Rotterdam Eye Study, and the Blue Mountains Eye Study[39]; Reykjavik = Reykjavik Eye Study[41]; SiMES = Singapore Malay Eye Study[31]; Shihpai = Shihpai Eye Study[28].

persons (1.1% and 0.3%, respectively).[5] Polypoidal choroidal vasculopathy lesions have been known to be more prevalent in black persons compared with whites,[40] which seems to be similar to that among Asians.

Further, if PCV was considered to differ substantially from more typical neovascular AMD, then racial/ethnic differences in late AMD prevalence would presumably be more apparent. This notion is supported by the observation that the prevalence of late AMD in Asian women was much lower than in both Asian men and white women. To clearly understand the epidemiology of late AMD subtypes and the influences of possible variants such as PCV, future studies are needed that include specific examinations such as fluorescein and indocyanine green angiography, or at least optical coherence tomography, to classify AMD subtypes and identify the presence of PCV in older Asian populations.

Limitations of this study should be discussed. First, although we standardized the prevalence rates by age distribution, we could not adjust for other AMD risk factors, such as smoking status and genetic predisposition, which might have important influences on AMD prevalence. Second, available publications/studies were from only 4 countries/regions/ethnic groups. This, the prevalence estimates for other Asian regions/ethnicities remain to be determined. Third, we had no reliable data with an appropriate number of subjects on the prevalence of specific late AMD subtypes (i.e., neovascular AMD compared with geographic atrophy).

Clinical Recommendations

In summary, we found that the age-specific prevalence of late AMD is comparable between Asians and whites but that early AMD rates are lower in Asians than whites (A, II). We found substantially higher rates of late AMD prevalence in Asian men compared with Asian women or with white men, which could reflect the higher proportion of PCV, particularly in Asian men (B, III). Additional epidemiologic and clinical studies in Asian populations are warranted to assess if there are racial/ethnicity differences in late AMD lesion subtypes (i.e., neovascular AMD vs. geographica atrophy) or with "Asian forms of AMD" (i.e., PCV). In addition, cross-validation of AMD grading results and pooling of individual data based on standardized grading system and methodology will provide even more precise estimates for AMD prevalence in Asians. These new studies should assume a high priority.

References

1. Pascolini D, Mariotti SP, Pokharel GP, et al. 2002 global update of available data on visual impairment: a compilation of population-based prevalence studies. Ophthalmic Epidemiol 2004;11:67–115.
2. Schachat AP, Hyman L, Leske MC, et al, Barbados Eye Study Group. Features of age-related macular degeneration in a black population. Arch Ophthalmol 1995;113:728–35.
3. Friedman DS, Katz J, Bressler NM, et al. Racial differences in the prevalence of age-related macular degeneration: the Baltimore Eye Survey. Ophthalmology 1999;106:1049–55.
4. Klein R, Klein BE, Knudtson MD, et al. Prevalence of age-related macular degeneration in 4 racial/ethnic groups in the Multi-ethnic Study of Atherosclerosis. Ophthalmology 2006; 113:373–80.
5. Bressler SB, Munoz B, Solomon SD, West SK, Salisbury Eye Evaluation (SEE) Study Team. Racial differences in the prevalence of age-related macular degeneration: the Salisbury Eye Evaluation (SEE) Project. Arch Ophthalmol 2008;126:241–5.
6. United Nations Population Division. World Population Prospects: The 2008 Revision Population Database. Panel 2: Detailed Data. Available at: http://esa.un.org/unpp/index.asp?panel=2. Accessed May 25, 2009.
7. Jager RD, Mieler WF, Miller JW. Age-related macular degeneration. N Engl J Med 2008;358:2606–17.
8. Yuzawa M, Tamakoshi A, Kawamura T, et al. Report on the nationwide epidemiological survey of exudative age-related macular degeneration in Japan. Int Ophthalmol 1997;21:1–3.
9. Klein R, Klein BE, Cruickshanks KJ. The prevalence of age-related maculopathy by geographic region and ethnicity. Prog Retin Eye Res 1999;18:371–89.
10. Oshima Y, Ishibashi T, Murata T, et al. Prevalence of age related maculopathy in a representative Japanese population: the Hisayama study. Br J Ophthalmol 2001;85:1153–7.
11. Kawasaki R, Wang JJ, Aung T, et al, Singapore Malay Eye Study Group. Prevalence of age-related macular degeneration in a Malay population: the Singapore Malay Eye Study. Ophthalmology 2008;115:1735–41.
12. Kawasaki R, Wang JJ, Ji GJ, et al. Prevalence and risk factors for age-related macular degeneration in an adult Japanese population: the Funagata study. Ophthalmology 2008;115: 1376–81.
13. Chen SJ, Cheng CY, Peng KL, et al. Prevalence and associated risk factors of age-related macular degeneration in an elderly Chinese population in Taiwan: the Shihpai Eye Study. Invest Ophthalmol Vis Sci 2008;49:3126–33.
14. Krishnaiah S, Das T, Nirmalan PK, et al. Risk factors for age-related macular degeneration: findings from the Andhra Pradesh Eye Disease Study in South India. Invest Ophthalmol Vis Sci 2005;46:4442–9.

15. Krishnaiah S, Das PT, Kovai V, Rao GN. Associated factors for age-related maculopathy in the adult population in southern India: the Andhra Pradesh Eye Disease Study. Br J Ophthalmol 2009;93:1146–50.
16. Li Y, Xu L, Jonas JB, et al. Prevalence of age-related maculopathy in the adult population in China: the Beijing eye study. Am J Ophthalmol 2006;142:788–93.
17. Gupta SK, Murthy GV, Morrison N, et al. Prevalence of early and late age-related macular degeneration in a rural population in northern India: the INDEYE feasibility study. Invest Ophthalmol Vis Sci 2007;48:1007–11.
18. Sho K, Takahashi K, Yamada H, et al. Polypoidal choroidal vasculopathy: incidence, demographic features, and clinical characteristics. Arch Ophthalmol 2003;121:1392–6.
19. Maruko I, Iida T, Saito M, et al. Clinical characteristics of exudative age-related macular degeneration in Japanese patients. Am J Ophthalmol 2007;144:15–22.
20. Kondo N, Honda S, Ishibashi K, et al. LOC387715/*HTRA1* variants in polypoidal choroidal vasculopathy and age-related macular degeneration in a Japanese population. Am J Ophthalmol 2007;144:608–12.
21. Lee KY, Vithana EN, Mathur R, et al. Association analysis of *CFH, C2, BF,* and *HTRA1* gene polymorphisms in Chinese patients with polypoidal choroidal vasculopathy. Invest Ophthalmol Vis Sci 2008;49:2613–9.
22. Kondo N, Honda S, Ishibashi K, et al. Elastin gene polymorphisms in neovascular age-related macular degeneration and polypoidal choroidal vasculopathy. Invest Ophthalmol Vis Sci 2008;49:1101–5.
23. Kondo N, Honda S, Kuno S, Negi A. Coding variant I62V in the complement factor H gene is strongly associated with polypoidal choroidal vasculopathy. Ophthalmology 2009;116: 304–10.
24. Cackett P, Wong D, Yeo I. A classification system for polypoidal choroidal vasculopathy. Retina 2009;29:187–91.
25. Nakashizuka H, Mitsumata M, Okisaka S, et al. Clinicopathologic findings in polypoidal choroidal vasculopathy. Invest Ophthalmol Vis Sci 2008;49:4729–37.
26. Eandi CM, Ober MD, Freund KB, et al. Selective photodynamic therapy for neovascular age-related macular degeneration with polypoidal choroidal neovascularization. Retina 2007;27:825–31.
27. Gomi F, Ohji M, Sayanagi K, et al. One-year outcomes of photodynamic therapy in age-related macular degeneration and polypoidal choroidal vasculopathy in Japanese patients. Ophthalmology 2008;115:141–6.
28. Tsuchiya D, Yamamoto T, Kawasaki R, Yamashita H. Two-year visual outcomes after photodynamic therapy in age-related macular degeneration patients with or without polypoidal choroidal vasculopathy lesions. Retina 2009;29:960–5.
29. Gomi F, Sawa M, Sakaguchi H, et al. Efficacy of intravitreal bevacizumab for polypoidal choroidal vasculopathy. Br J Ophthalmol 2008;92:70–3.
30. Klein R, Davis MD, Magli YL, et al. The Wisconsin age-related maculopathy grading system. Ophthalmology 1991;98: 1128–34.
31. International ARM Epidemiological Study Group. An international classification and grading system for age-related maculopathy and age-related macular degeneration. Surv Ophthalmol 1995;39:367–74.
32. de Weerd M, Greving JP, de Jong AW, et al. Prevalence of asymptomatic carotid artery stenosis according to age and sex: systematic review and metaregression analysis. Stroke 2009; 40:1105–13.
33. Ahmad OB, Boschi-Pinto C, Lopez AD, et al. Age standardization of rates: A new WHO standard. Geneva: World Health Organization; 2000. GPE discussion paper series: No. 31. Available at: http://www.who.int/healthinfo/paper31.pdf. Accessed September 26, 2009.
34. Oguido AP, Casella AM, Matsuo T, et al. Prevalence of age-related macular degeneration in Japanese immigrants and their descendants living in Londrina (PR) - Brazil. Arq Bras Oftalmol 2008;71:375–80.
35. Li Y, Xu L, Wang YX, et al. Prevalence of age-related maculopathy in the adult population in China: the Beijing eye study [letter]. Am J Ophthalmol 2008;146:329.
36. Song SJ, Youm DJ, Chang Y, Yu HG. Age-related macular degeneration in a screened Korean population: prevalence, risk factors and subtypes. Ophthalmic Epidemiol 2009;16: 304–10.
37. Roh MI, Kim JH, Byeon SH, et al. Estimated prevalence and risk factor for age-related maculopathy. Yonsei Med J 2008; 49:931–41.
38. Klaver CC, Assink JJ, van Leeuwen R, et al. Incidence and progression rates of age-related maculopathy: the Rotterdam Study. Invest Ophthalmol Vis Sci 2001;42:2237–41.
39. Liu Y, Wen F, Huang S, et al. Subtype lesions of neovascular age-related macular degeneration in Chinese patients. Graefes Arch Clin Exp Ophthalmol 2007;245:1441–5.
40. Ciardella AP, Donsoff IM, Huang SJ, et al. Polypoidal choroidal vasculopathy. Surv Ophthalmol 2004;49:25–37.

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[1] Centre for Eye Research Australia, Royal Victorian Eye and Ear Hospital, University of Melbourne, Australia.

[2] Department of Ophthalmology and Visual Science, Yamagata University Faculty of Medicine, Japan.

[3] Department of Ophthalmology, Graduate School of Medical Sciences, University of Kyusyu, Japan.

[4] Department of Ophthalmology, Kangbuk Samsung Hospital, Sungkyunkwan University School of Medicine, Seoul, Korea.

[5] Department of Ophthalmology, Taipei Veterans General Hospital, Taiwan.

[6] Department of Ophthalmology, Faculty of Clinical Medicine Mannheim, University of Heidelberg, Mannheim, Germany.

[7] Centre for Vision Research, Westmead Millennium Institute, University of Sydney, Australia.

[8] Singapore Eye Research Institute, Yong Loo Lin School of Medicine, National University of Singapore, Singapore.

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Correspondence:
Tien Yin Wong, MD, MPH, PhD, Singapore Eye Research Institute, Singapore National Eye Centre, 11 Third Hospital Avenue, Singapore 168751, Singapore. E-mail: ophwty@nus.edu.sg.

The Prevalence of Retinal Vein Occlusion: Pooled Data from Population Studies from the United States, Europe, Asia, and Australia

*Sophie Rogers, BSc, MEpid,[1] Rachel L. McIntosh, BOrth Grad Dip Journ,[1] Ning Cheung, MBBS,[1] Lyndell Lim, MBBS, FRANZCO,[1] Jie Jin Wang, PhD,[1,2] Paul Mitchell, MD, PhD,[2] Jonathan W. Kowalski, PharmD,[3] Hiep Nguyen, MPH,[3] Tien Y. Wong, MD, PhD,[1,4] for the International Eye Disease Consortium**

Objective: To summarize the prevalence of retinal vein occlusion (RVO) from studies in the United States, Europe, Asia, and Australia.

Design: Pooled analysis using individual population-based data.

Participants: Individual participant data from population-based studies around the world that had ascertained RVO from fundus photographs.

Methods: Each study provided data on branch RVO and central RVO by age, sex, and ethnicity. Prevalence rates were directly age and sex standardized to the 2008 world population aged 30 years and older. Estimates were calculated by study and, after pooling, by ethnicity. Summary estimates included studies in which RVO was assessed from fundus photographs on ≥2 fields of both eyes.

Main Outcome Measures: Any RVO, CRVO, or BRVO.

Results: The combined pooled data contained 68,751 individuals from 15 studies, with participants' ages ranging from 30 to 101 years. In analyses of 11 studies that assessed ≥2 fundus fields of both eyes (n=49,869), the age- and sex-standardized prevalence was 5.20 per 1000 (confidence interval [CI], 4.40–5.99) for any RVO, 4.42 per 1000 (CI, 3.65–5.19) for BRVO, and 0.80 per 1000 (CI, 0.61–0.99) for CRVO. Prevalence varied by race/ethnicity and increased with age, but did not differ by gender. The age- and sex-standardized prevalence of any RVO was 3.7 per 1000 (CI, 2.8–4.6) in whites (5 studies), 3.9 per 1000 (CI, 1.8–6.0) in blacks (1 study), 5.7 per 1000 (CI, 4.5–6.8) in Asians (6 studies), and 6.9 per 1000 (CI, 5.7–8.3) in Hispanics (3 studies). Prevalence for CRVO was lower than BRVO in all ethnic populations. On the basis of these data, an estimated 16.4 million (CI, 13.9–18.9) adults are affected by RVO, with 2.5 million (CI, 1.9–3.1) affected by CRVO and 13.9 million (CI, 11.5–16.4) affected by BRVO. Study limitations include non-uniform sampling frames in identifying study participants and in acquisition and grading of RVO data.

Conclusions: Our study provides summary data on the prevalence of RVO and suggests that approximately 16 million people may have this condition. Research on preventive and treatment strategies for this sight-threatening eye disease is needed.

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**Group members of the International Eye Disease Consortium are listed in Appendix 1, available at http://aaojournal.org.*

Retinal vein occlusion (RVO) is one of the most common causes of acquired retinal vascular abnormality in adults and a frequent cause of visual loss. Despite being recognized at least as early as 1855[1] and the subject of more than 3000 publications, there are few data on the prevalence of RVO in the general population, with current estimates derived largely from studies in white populations.[2–4] More recently, population data have emerged from other racial/ethnic groups, such as in Chinese,[5] Hispanics,[6] and Asian Malays.[7] The reported prevalence of RVO varies between 0.3%[4] and 1.6%.[3] The variability in prevalence rates is likely related to the small number of RVO cases in any single study, differing study methodologies (e.g., retinal photography), and possible racial/ethnic differences in distributions of RVO risk factors.

Because of these limitations, estimates of RVO prevalence have been imprecise. Furthermore, most single studies rarely reported on the prevalence of different RVO subtypes, namely, central retinal vein occlusion (CRVO) and branch retinal vein occlusion (BRVO), which are important to distinguish because they have different risk factors,[8,9] prognosis, and treatment.[10–12]

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In this report, we combined individual-level data from 15 major population-based studies around the world and estimated the prevalence of BRVO and CRVO and their relationships with age, gender, and race/ethnicity.

Materials and Methods

Study Selection and Inclusion

A systematic review of the literature for all relevant population-based studies that undertook retinal photography was conducted. We searched all English language and human subject articles using a keyword search of MEDLINE (1950 to November 13, 2008), EMBASE (<1966 to December 18, 2008), Current Contents (1999 to December 18, 2008), and the Cochrane Library (to December 18, 2008) using the following search terms: retinal photography OR retinal images OR fundus photography AND population based. A total of 1585 citations were identified as of December 18, 2008. Irrelevant and duplicate articles were excluded on the basis of a review of the titles and abstracts. The full text of the remaining articles was reviewed to ensure all studies met the inclusion criteria and did not meet the exclusion criteria. In addition, we further consulted with experts to identify population-based studies that had assessed the presence of RVO from fundus photographs, but which may not have published results examining RVO or in which assessment of RVO from retinal photographs was still ongoing.

Studies were excluded if they were not population-based (i.e., excluding studies of clinic patient samples), fundus photographs were not taken or were not taken for all subjects, or images were not graded for RVO or the grading did not distinguish RVO subtype. Studies included in this review were those population-based studies in which RVO diagnosis was based on retinal photographic grading by a trained grader. We identified 21 population-based studies in which fundus photographs were potentially graded for RVO; of these, 7 had reported on the prevalence of RVO.[2–7]

We then contacted the lead investigators of the identified studies to request collaboration. Collaborators were requested to provide data on the following: presence of RVO and subtypes (CRVO, BRVO), age, sex, and race/ethnicity. All studies had prior institutional review board approval and provided appropriately de-identified data for analysis.

In total, investigators from 15 of the 21 identified studies provided data: Atherosclerosis Risk in Communities Study, Beaver Dam Eye Study, Cardiovascular Health Study (CHS), Los Angeles Latino Eye Study, Multi-Ethnic Study of Atherosclerosis (MESA), and the Arizona Project on Vision, Evaluation, Research from the United States; EUREYE and Rotterdam Eye Study from Europe; Beijing Eye Study, Funagata Study, Handan Eye Study, Hisayama Study, Shihpai Eye Study, and Singapore Malay Eye Study from Asia; and the Blue Mountains Eye Study from Australia. Investigators of the remaining 6 studies that did not contribute data to this study did not want to participate, did not respond, or could not be contacted.

Definition of Retinal Vein Occlusion

All 15 studies had retinal photography performed to a standardized protocol. All photographs were graded for RVO on the basis of standard definitions, and the majority of studies used 1 of 4 fundus photograph reading centers: United States (Ocular Epidemiology Reading Center at the University of Wisconsin-Madison), The Netherlands (Rotterdam Grading Centre), and Australia (Centre for Vision Research, University of Sydney and the Centre for Eye Research Australia, University of Melbourne), where the RVO grading procedures were standardized.

Central retinal vein occlusion was defined to be present if there was retinal edema, optic disc hyperemia or edema, scattered superficial and deep retinal hemorrhages, and venous dilation.[2–7] Long-standing CRVO was defined to be present if occluded or sheathed retinal veins or vascular anastomoses at the optic disc were detected. Branch retinal vein occlusion was defined as the presence of localized retinal edema, superficial and deep retinal hemorrhages, intraretinal microvascular abnormalities or anastomotic vessels, and venous dilation or venous sheathing within a sector of the retina corresponding to the obstructed vein.[2–7] Retinal vein occlusion was defined as present when either BRVO or CRVO was detected in at least 1 eye.

Appraisal of Quality of Studies

Because there were no established guidelines on evaluating prevalence studies, we adopted and further modified the quality assessment criteria by de Weerd et al.[13] The quality of all studies was assessed for the following attributes:

- Representation of the general population, whereby participants selected should ideally by representative of the general population. Methods of achieving this may involve using population registries, inhabitants of a defined area, and people registered with a general practice. Participants attending health checkups may be biased and only cover certain population groups.
- Appropriate recruitment of the population. Recruitment was considered appropriate if recruitment of participants was random or consecutive rather than performed for convenience.
- Adequate response rate (>70%).
- Objective documentation of the outcome, in this case, documentation by retinal photography performed according to standardized protocols and graded according to standard definitions.

A score of 3 or higher was considered adequate quality.

Statistical Analysis

Data from each study were checked for consistency in variable definitions before pooling. Race/ethnicity was categorized as Asian (Chinese, Chinese-American, Malay, people of Asian origin and Europeans of Indian, Indonesian, or Asian origin), black (African-Americans), Hispanic (Hispanic-Americans), and white (Europeans, and those of European origin).

Study-specific and pooled-data estimation of RVO prevalence rates were obtained using the direct method of age-sex-standardization to the 2008 world population aged 30 years and older.[14] This standardization involved 6 age categories (30–39 years, 40–49 years, 50–59 years, 60–69 years, 70–79 years, and ≥80 years) in men and women separately. The calculation of 95% confidence intervals (CIs) for the standardized prevalence rates used a normal approximation and Breslow-Day standard errors, after being modified to use a binomial assumption for the variance of the crude stratum-specific rates.[15] Crude prevalence rates per 1000 and Agresti-Coull modified Wald CIs were also calculated.

Initial analyses included data from all 15 studies. Subsequent analyses used only the 11 studies that had assessed RVO with 2 or more retinal photographic fields from both eyes of participants (considered to have high sensitivity in detection).

Supplementary analysis included logistic regression of the effect of number of photographic fields per eye and the number of eyes with photographs taken per participant and the effect of pharmacologic mydriasis on the likelihood of an RVO diagnosis (adjusted for study, age, sex, and ethnicity).

Results

Overall, we collated data for 68,751 participants from 15 studies from the United States, Europe, Asia, and Australia. Of these participants, 43.7% were male, 48.4% were white, 27.1% were Asian, 17.2% were Hispanic, and 7.2% were black. Summary characteristics of each of the included studies are presented in Table 1; detailed characteristics of the participants in each of these studies have been described in previous publications (Table 1).

The majority of studies were conducted in only 1 ethnic group, except for the Atherosclerosis Risk in Communities Study, CHS, MESA, and Rotterdam studies, which had more than 1 ethnic group. Of the 15 studies, 11 assessed RVO from 2 or more retinal photographic fields of both eyes of each subject; of these 11 studies, retinal photographs were taken after pharmacologic mydriasis in 10 (the MESA differed). Of the studies that had 2 retinal fields photographed, 1 was centered at the optic disc (Early Treatment for Diabetic Retinopathy Study Field 1) and the other was centered on the macula (Early Treatment for Diabetic Retinopathy Study Field 2). Cameras varied between studies, ranging from a stereoscopic film-based mydriatic camera (Zeiss FF3 camera, Carl Zeiss, Oberkochen, Germany) to a digital non-mydriatic retinal camera (Canon CR-DGi with a 10D SLR backing, Canon, Tokyo, Japan).

The age- and sex-standardized prevalence (per 1000 persons) was 3.77 (CI, 3.08–4.46) for BRVO and 0.65 (CI, 0.49–0.80) for CRVO in the pooled analysis (Table 2). The standardized prevalence rates for CRVO in individual studies varied from 0.04 per 1000 (CI, 0–0.12) in CHS to 1.59 per 1000 (CI, 0.83–2.35) in the Blue Mountains Eye Study. Corresponding standardized BRVO prevalence ranged from 0.26 (CI, 0.07–0.45) in CHS to 9.32 (CI, 5.96–12.67) in Hisayama. There was no discernible difference between the age-standardized prevalence rates in men and women.

Analyses confined to 11 studies that assessed 2 or more fields of both eyes, involving 49,869 participants, generated slightly higher prevalence estimates: Prevalence was 4.42 (CI, 3.65–5.19) for BRVO, 0.80 (CI, 0.61–0.99) for CRVO, and 5.20 (CI, 4.40–5.99) for any RVO per 1000 adults. By using these prevalence rates and the 2008 world population,[14] we estimated that 16.4 million (CI, 13.9–18.9) adults worldwide are affected by RVO, 2.5 million (CI, 1.9–3.1) adults are affected by CRVO, and 13.9 million (CI, 11.5–16.4) adults are affected by BRVO. Analyses repeated including only the 10 studies in which pharmacologic mydriasis was performed resulted in similar estimates (data not shown).

The crude prevalence of all types of RVO increased with age (all P for trend <0.001; Table 3). This pattern was seen overall and in men and women separately. In studies that undertook photography of 2 or more fields in both eyes per subject, the age- and sex-standardized prevalence of BRVO varied across ethnic groups, with Asian and Hispanic groups exhibiting the highest prevalence and whites exhibiting the lowest prevalence (Fig 1). There were no obvious ethnic differences in CRVO prevalence.

Discussion

The pooling of individual-level data from studies from the United States, Europe, Asia, and Australia allowed us to estimate more precisely the prevalence of RVO in the general adult population. On the basis of approximately 50,000 people from 11 studies that had assessed RVO from fundus photographs of 2 or more fields taken from each of the 2 eyes per participant, we estimate an age- and sex-standardized prevalence of 4.42 per 1000 persons for BRVO and 0.80 per 1000 persons for CRVO. The prevalence of RVO was similar between men and women, and increased with age. The prevalence of BRVO was highest in Asians and Hispanics and lowest in whites.

Previous population-based studies on RVO have provided rough estimates of RVO prevalence in their respective countries, often based on data from 1 region or city.[2–7] This is the first synthesis of individual-level data from major population-based studies on RVO, with a sufficiently large sample to allow more precise estimation by age, sex, and ethnicity. The studies included had distinguished BRVO and CRVO using standardized retinal photographic grading; thus, we were able to provide prevalence estimates by subtypes of vein occlusion. Projected to the world population, approximately 16 million people may have occlusive venous disease in at least 1 eye. This estimated projection should be interpreted with caution because we did not have estimates of RVO from population-based studies in South America or Africa.

In keeping with findings from previous studies,[2–7] our study found that age is an important risk factor for RVO.[16] This likely reflects an increase in arteriosclerosis and in age-related vascular (e.g., systemic hypertension)[17] and ocular (e.g., glaucoma or increased intraocular pressure) risk factors.[9]

Overall, these pooled data show the highest prevalence of BRVO in Asians and Hispanics and the lowest prevalence in whites, although the overlapping CIs suggest racial/ethnic differences are not statistically significant. In the MESA,[6] the only study with 4 racial ethnic groups examined in 1 study, the crude prevalence of any RVO was similar across whites, blacks, Chinese, and Hispanics. It is worth noting that in the MESA, sample sizes of each ethnic group were relatively small, particularly the Chinese subgroup (n=724), and that all participants were US residents who were free of clinical cardiovascular disease (i.e., generally healthier study samples). Therefore, the MESA might not be sufficiently powered to detect meaningful ethnic difference in RVO prevalence and should not be expected to represent different ethnic groups outside the United States. Other studies of multiple ethnic samples, as a single study, also did not have sufficient numbers of RVO cases to examine racial/ethnic differences by RVO subtypes. The higher prevalence of BRVO in some racial/ethnic groups may reflect different population distributions of RVO risk factors. For example, the prevalence of hypertension and uncontrolled hypertension is reported to be higher in Asians[18] and Hispanics[19] than in whites.[20,21]

Strengths of the present study include the uniquely large sample size, inclusion of studies from different ethnic populations around the world, estimates of RVO subtypes (BRVO and CRVO), and inclusion of only those studies that used photographic documentation. These data provide a more precise estimate of the prevalence in the general population because they included RVO cases of both known, presumably symptomatic, and unknown (undiagnosed) causes. However, pooling data from many sources has many potential sources of heterogeneity.[22] First, there could be substantial variations in study inclusion criteria, sample selection, and participation rates. Second, there were

Table 1. Characteristics of

	Country	N Subjects (% Male)	Mean Age (Range)	Ethnicity*
ARIC[4,23]	USA	12,604 (44.6)	59.9 (49–73)	77% were white, 23% were black
BDES[2]	USA	4896 (43.8)	62.1 (43–86)	100% were white
Beijing Eye Study[5,24]	China	4439 (43.6)	56.2 (40–101)	100% were Asian (Chinese)
BMES[3,25]	Australia	3651 (43.3)	66.2 (45–97)	99% were white
CHS[4,26]	USA	4249 (37.9)	78.7 (69–101)	83% were white, 17% were black
EUREYE Study[27]	European	4753 (44.8)	72.7 (64–99)	100% were white
Funagata Study[28]	Japan	1638 (43.5)	60.0 (34–96)	100% were Asian (Japanese)
HandanEye Study[29,30]	China	6716 (46.5)	52.0 (30–97)	100% were Asian (Chinese)
Hisayama Study[31]	Japan	1775 (38.8)	61.9 (40–96)	100% were Asian (Japanese)
LALES[32]	USA	6357 (41.4)	54.9 (40–98)	100% were Hispanic
MESA[6,33]	USA	6176 (47.7)	63.5 (46–87)	39% were white, 27% were black, 22% were Hispanic, 12% were Asian (Chinese)
Proyecto VER Study[34]	USA	4774 (38.8)	56.9 (40–96)	100% were Hispanic
Rotterdam Study[35,36]	The Netherlands	6418 (40.7)	69.0 (55–99)	98% were white, 1% were Asian ("Asian," Indonesian, Indian)
ShihpaiEye Study[37]	Taiwan	1058 (62.0)	71.8 (65–90)	100% were Asian (Chinese)
SiMES[7,38]	Singapore	3280 (48.1)	58.7 (40–80)	100% were Asian (Malay)

AGC = Australian Grading Centre (Centre for Vision Research, University of Sydney and the Centre for Eye Research Australia, University of Cardiovascular Health Study; LALES = Los Angeles Latino Eye; OERC = Ocular Epidemiology Reading Center at the University of Wisconsin;
*Totals for ethnicity may not equal 100%; some studies had subjects from other ethnic groups not included in this analysis.
†The quality criteria failed: 1 = representation of the general population, 2 = appropriate recruitment of the population (random or consecutive), 3 = criteria.

differences in methods used to detect and diagnose RVO across studies, including the use of mydriasis, choice of retinal photographic fields per eye, number of eyes examined per subject, photographic quality, case definitions (e.g., questionable or old RVOs), and the exclusion of other ocular pathologies. Third, given that most of the included studies are of subjects from 1 ethnic group, observed ethnic differences in prevalence should be interpreted with caution

Table 2. Age- and Sex-Standardized Prevalence of Central, Branch, and Any Retinal Vein Occlusion by Study

			CRVO		BRVO		Any RVO		Standardized Prevalence* (/1000)		
	Eyes/ Subject	Field/ Eye	*N* (*Total*)	*N* (*RVO*)	*N* (*Total*)	*N* (*RVO*)	*N* (*Total*)	*N* (*RVO*)	CRVO	BRVO	Any RVO
All (15 studies)	Any	Any	68,700	92	68,721	466	68,751	555	0.65 (0.49–0.80)	3.77 (3.08–4.46)	4.40 (3.69–5.11)
All (11 studies)	Both	≥2	49,818	83	49,839	395	49,869	475	0.80 (0.61–0.99)	4.42 (3.65–5.19)	5.20 (4.40–5.99)
Men (15 studies)	Any	Any	30,318	39	30,329	214	30,340	251	0.58 (0.35–0.80)†	3.19 (2.66–3.71)†	3.74 (3.17–4.31)†
Women (15 studies)	Any	Any	38,382	53	38,392	252	38,411	304	0.72 (0.50–0.93)†	4.33 (3.07–5.60)†	5.04 (3.75–6.32)†
Men (11 studies)	Both	≥2	22,170	35	22,181	180	22,192	213	0.71 (0.43–0.99)†	3.76 (3.11–4.40)†	4.43 (3.74–5.13)†
Women (11 studies)	Both	≥2	27,648	48	27,658	215	27,677	262	0.89 (0.61–1.16)†	5.07 (3.69–6.45)†	5.93 (4.52–7.34)†
By Study											
ARIC	1 eye	1	12,604	4	12,604	19	12,604	23	0.10 (0–0.19)	0.45 (0.24–0.65)	0.54 (0.32–0.77)
BDES	Both	3	4792	8	4792	29	4792	37	0.99 (0.21–1.78)	2.82 (1.65–4.00)	3.82 (2.40–5.23)
Beijing Eye Study	Both	2	4335	5	4335	31	4439	35	0.70 (0.04–1.35)	4.67 (2.48–6.85)	5.27 (2.99–7.55)
BMES	Both	6	3492	17	3525	50	3542	67	1.59 (0.83–2.35)	5.63 (3.94–7.32)	7.14 (5.31–8.98)
CHS	1 eye	1	2824	1	2824	7	2824	8	0.04 (0–0.12)	0.26 (0.07–0.45)	0.30 (0.09–0.50)
EUREYE Study	Both	2	4753	9	4753	30	4753	39	0.42 (0.12–0.72)	1.48 (0.91–2.05)	1.90 (1.25–2.54)
Funagata Study	1 eye	1	1502	1	1502	8	1502	9	0.21 (0–0.64)	3.87 (0.13–7.61)	4.09 (0.32–7.85)
Handan Eye Study	Both	2	6716	6	6716	52	6716	58	0.55 (0.10–0.99)	6.16 (4.30–8.01)	6.70 (4.79–8.61)
Hisayama Study	Both	1	1775	3	1775	35	1775	38	0.77 (0–1.64)	9.32 (5.96–12.67)	10.09 (6.62–13.55)
LALES	Both	3	6013	7	6011	51	6013	58	0.79 (0.2–1.39)	6.02 (4.31–7.73)	6.75 (4.95–8.55)
MESA	Both	2	6141	7	6132	35	6142	42	0.38 (0.09–0.66)	2.87 (1.56–4.19)	3.24 (1.90–4.58)
Proyecto VER Study	Both	3	2909	10	2908	48	2909	58	1.52 (0.54–2.50)	6.85 (4.89–8.81)	8.37 (6.17–10.56)
Rotterdam Study	Both	2	6418	6	6418	34	6418	39	0.39 (0.02–0.75)	1.60 (0.98–2.22)	1.94 (1.23–2.64)
Shihpai Eye Study	Both	2	1058	3	1058	19	1058	22	0.38 (0–0.84)	3.45 (1.72–5.18)	3.83 (2.04–5.62)
SiMES	Both	2	3265	5	3265	18	3265	22	0.82 (0.07–1.57)	2.82 (1.46–4.19)	3.56 (2.01–5.11)

ARIC = Atherosclerosis Risk in Communities Study; BDES = Beaver Damn Eye Study; BMES = Blue Mountains Eye Study; BRVO = branch retinal vein occlusion; CHS = Cardiovascular Health Study; CRVO = central retinal vein occlusion; LALES = Los Angeles Latino Eye; n = study sample size; RVO = retinal vein occlusion; SiMES = Singapore Malay Eye Study; VER = Vision Evaluation and Research.
*Prevalence per 1000 adults. Prevalence has been directly age- and sex-standardized to the 2008 world population aged ≥ 30 years (population data extracted from Ref. 14).
†Denotes sex-specific estimates of prevalence are directly age standardized using the method and population as above.

Included Studies

Eyes/Subject	Fields per Eye (Degree, Dilation, Camera Type)	Image Grading Center	No. of Quality Criteria†
1 eye	1 field (45 degrees undilated, non-mydriatic, non-stereo)	Graded OERC	3 (3)
Both	≥3† fields (30 degrees dilated, mydriatic, 2 stereo, ≥1 non-stereo)	Graded OERC	4
Both	2 fields (45 degrees dilated, mydriatic, non-stereo)	Graded at study site; confirmed AGC	4
Both	6 fields (30 degrees dilated, mydriatic, 2 stereo, 4 non-stereo)	Graded AGC	4
1 eye	1 field (45 degrees undilated, non-mydriatic, non-stereo)	Graded OERC	
Both	2 fields (35 degrees dilated, mydriatic, stereo)	Graded RGC	3 (3)
1 eye	1 field (45 degrees undilated, non-mydriatic, non-stereo)	Graded AGC	3 (3)
Both	2 fields (45 degrees dilated, non-mydriatic, non-stereo)	Graded at study site	4
Both	1 field (45 degrees dilated, non-mydriatic, non-stereo)	Graded at study site	3 (3)
Both	≥3† fields (30 degrees dilated, mydriatic, stereo)	Graded OERC	4
Both	2 fields (45 degrees undilated, non-mydriatic, non-stereo)	Graded OERC	
Both	3 fields (30 degrees dilated, mydriatic, stereo)	Graded OERC	4
Both	2 fields (35 degrees dilated, mydriatic, stereo)	Graded RGC	3 (3)
Both	≥2† fields (35 degrees dilated, mydriatic, non-stereo)	Graded at study site	3 (3)
Both	2 fields (45 degrees dilated, non-mydriatic, non-stereo)	Graded AGC	4

Melbourne; ARIC = Atherosclerosis Risk in Communities Study; BDES = Beaver Damn Eye Study; BMES = Blue Mountains Eye Study; CHS = RGC = Rotterdam Grading Centre; SiMES = Singapore Malay Eye Study; VER = Vision Evaluation and Research.

adequate response rate (>70%), 4 = objective outcome measurement by retinal photography performed to standard protocol and graded to standard

because these differences could be mostly due to differing study methodologies rather than true ethnic differences. Furthermore, definitions of particular ethnic group may differ across studies. For example, most studies used self-reported ethnicity, whereas the Rotterdam study used grandparental country of birth to define ethnicity. Also, all of the included Hispanic participants were US residents, whereas the majority of Asian participants reside in Asian countries.

Table 3. Crude Prevalence of Central, Branch, and Any Retinal Vein Occlusion By Age and Gender

	Men			Women			All		
	N (Total)	*n (RVO)*	*Crude Prevalence/1000 (95% CI)*	*N (Total)*	*n (RVO)*	*Crude Prevalence/1000 (95% CI)*	*N (Total)*	*n (RVO)*	*Crude Prevalence/1000 (95% CI)*
CRVO									
Age 30–39 yrs	560	0	0 (0–0)	676	0	0 (0–0)	1236	0	0 (0–0)
Age 40–49 yrs	3184	1	0.31 (0–0.93)	4101	1	0.24 (0–0.72)	7285	2	0.27 (0–0.65)
Age 50–59 yrs	5668	4	0.71 (0.01–1.4)	7297	5	0.69 (0.08–1.29)	12,965	9	0.69 (0.24–1.15)
Age 60–69 yrs	6658	8	1.2 (0.37–2.03)	7749	16	2.06 (1.05–3.08)	14,407	24	1.67 (1–2.33)
Age 70–79 yrs	5093	16	3.14 (1.6–4.68)	6069	16	2.64 (1.35–3.93)	11,162	32	2.87 (1.87–3.86)
Aged 80+ yrs	1067	6	5.62 (1.14–10.11)	1873	10	5.34 (2.04–8.64)	2940	16	5.44 (2.78–8.1)
P trend*			<0.001			<0.001			<0.001
BRVO									
Age 30–39 yrs	560	0	0 (0–0)	676	2	2.96 (0–7.05)	1236	2	1.62 (0–3.86)
Age 40–49 yrs	3184	5	1.57 (0.19–2.95)	4101	5	1.22 (0.15–2.29)	7285	10	1.37 (0.52–2.22)
Age 50–59 yrs	5673	26	4.58 (2.83–6.34)	7301	53	7.26 (5.31–9.21)	12,974	79	6.09 (4.75–7.43)
Age 60–69 yrs	6663	74	11.11 (8.59–13.62)	7756	60	7.74 (5.79–9.69)	14,419	134	9.29 (7.73–10.86)
Age 70–79 yrs	5095	65	12.76 (9.68–15.84)	6072	72	11.86 (9.14–14.58)	11,167	137	12.27 (10.23–14.31)
Aged 80+ yrs	1066	11	10.32 (4.25–16.39)	1869	24	12.84 (7.74–17.95)	2935	35	11.93 (8–15.85)
P trend*			<0.001			<0.001			<0.001
Any RVO									
Age 30–39 yrs	560	0	0 (0–0)	676	2	2.96 (0–7.05)	1236	2	1.62 (0–3.86)
Age 40–49 yrs	3184	6	1.88 (0.38–3.39)	4101	6	1.46 (0.29–2.63)	7285	12	1.65 (0.72–2.58)
Age 50–59 yrs	5673	30	5.29 (3.4–7.18)	7301	58	7.94 (5.91–9.98)	12,974	88	6.78 (5.37–8.2)
Age 60–69 yrs	6666	81	12.15 (9.52–14.78)	7758	75	9.67 (7.49–11.84)	14,424	156	10.82 (9.13–12.5)
Age 70–79 yrs	5100	80	15.69 (12.28–19.1)	6078	88	14.48 (11.48–17.48)	11,178	168	15.03 (12.77–17.29)
Aged 80+ yrs	1069	17	15.9 (8.4–23.4)	1880	34	18.09 (12.06–24.11)	2949	51	17.29 (12.59–22)
P trend*			<0.001			<0.001			<0.001

BRVO = branch retinal vein occlusion; CI = confidence interval; CRVO = central retinal vein occlusion; RVO = retinal vein occlusion.
Tables includes information from only those 11 studies that assessed ≥ 2 fields from both eyes per subject.
**P* relates to Cusick nonparametric test for trend across age groups.

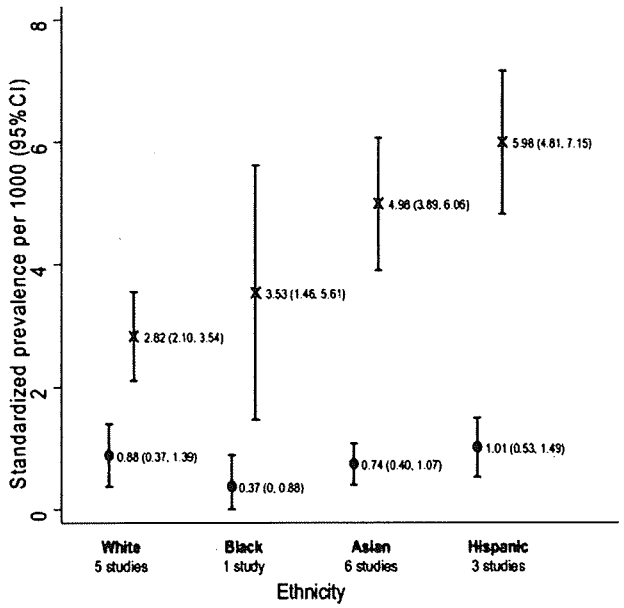

Figure 1. Age- and sex-standardized prevalence of CRVO and BRVO by ethnicity. Prevalence rates shown are per 1000 adults and include data from only those studies that assessed ≥2 fields of both eyes for each subject. Prevalence rates have been directly age- and sex-standardized to the 2008 world population aged ≥30 years (population data extracted from Ref. 15). CRVO (*circles*); BRVO (*crosses*); 95% CIs for prevalence estimates (*capped vertical lines*). BRVO = branch retinal vein occlusion; CI = confidence interval; CRVO = central retinal vein occlusion.

Finally, the 2 studies that have assessed RVO in blacks have been in America and not Africa.

In conclusion, by using pooled data involving approximately 50,000 participants from the United States, Europe, Asia, and Australia, our study shows that BRVO affects 4 per 1000 persons and that CRVO affects 0.8 per 1000 persons. On the basis of these rates, projected to the world population, approximately 16 million adults are affected by RVO. We show that the prevalence of both BRVO and CRVO increases significantly with age but does not differ by gender. Possible racial/ethnic differences in the prevalence of BRVO may reflect differences in the prevalence of RVO risk factors. Understanding the key roles of the principal systemic and ocular factors, particularly hypertension for both RVO subtypes and glaucoma for CRVO, across these different populations will be important. Finally, our data suggest the need for further research to better understand the epidemiology of RVO, which could translate into the design of appropriate preventive and treatment strategies.

References

1. Liebreich R. Ophthalmoskopische Notizen: Ueber die Farbe des Augengrundes. Albrecht Von Graefes Arch Ophthalmol 1855;1:333–43.
2. Klein R, Klein BE, Moss SE, Meuer SM. The epidemiology of retinal vein occlusion: the Beaver Dam Eye Study. Trans Am Ophthalmol Soc 2000;98:133–41.
3. Mitchell P, Smith W, Chang A. Prevalence and associations of retinal vein occlusion in Australia: the Blue Mountains Eye Study. Arch Ophthalmol 1996;114:1243–7.
4. Wong TY, Larsen EK, Klein R, et al. Cardiovascular risk factors for retinal vein occlusion and arteriolar emboli: the Atherosclerosis Risk in Communities & Cardiovascular Health studies. Ophthalmology 2005;112:540–7.
5. Liu W, Xu L, Jonas JB. Vein occlusion in Chinese subjects [letter]. Ophthalmology 2007;114:1795–6.
6. Cheung N, Klein R, Wang JJ, et al. Traditional and novel cardiovascular risk factors for retinal vein occlusion: the multiethnic study of atherosclerosis. Invest Ophthalmol Vis Sci 2008;49:4297–302.
7. Lim LL, Cheung N, Wang JJ, et al. Prevalence and risk factors of retinal vein occlusion in an Asian population. Br J Ophthalmol 2008;92:1316–9.
8. Hayreh SS, Zimmerman B, McCarthy MJ, Podhajsky P. Systemic diseases associated with various types of retinal vein occlusion. Am J Ophthalmol 2001;131:61–77.
9. O'Mahoney PR, Wong DT, Ray JG. Retinal vein occlusion and traditional risk factors for atherosclerosis. Arch Ophthalmol 2008;126:692–9.
10. Hayreh SS. Prevalent misconceptions about acute retinal vascular occlusive disorders. Prog Retin Eye Res 2005;24:493–519.
11. McIntosh RL, Mohamed Q, Saw SM, Wong TY. Interventions for branch retinal vein occlusion: an evidence-based systemic review. Ophthalmology 2007;114:835–54.
12. Mohamed Q, McIntosh RL, Saw SM, Wong TY. Interventions for central retinal vein occlusion: an evidence-based systematic review. Ophthalmology 2007;114:507–19, 524.
13. de Weerd M, Greving JP, de Jong AW, et al. Prevalence of asymptomatic carotid artery stenosis according to age and sex: systematic review and metaregression analysis. Stroke 2009; 40:1105–13.
14. U.S. Census Bureau. International Data Base. Total Midyear Population for the World: 1950-2050. Available at: http://www.census.gov/ipc/www/idb/region.php. Accessed July 7, 2009.
15. Keyfitz N. 3. Sampling variance of standardized mortality rates. Hum Biol 1966;38:309–17.
16. Verougstraete C. Is change of the vessel wall a risk factor for venous thrombosis [letter]? Lancet 1999;353:2158.
17. Wong TY, Mitchell P. The eye in hypertension. Lancet 2007; 369:425–35.
18. Leenen FH, Dumais J, McInnis NH, et al. Results of the Ontario survey on the prevalence and control of hypertension. CMAJ 2008;178:1441–9.
19. Read JG, Gorman BK. Racial/ethnic differences in hypertension and depression among US adult women. Ethn Dis 2007; 17:389–96.
20. Giles T, Aranda JM Jr, Suh DC, et al. Ethnic/racial variations in blood pressure awareness, treatment, and control. J Clin Hypertens (Greenwich) 2007;9:345–54.
21. Ostchega Y, Hughes JP, Wright JD, et al. Are demographic characteristics, health care access and utilization, and comorbid conditions associated with hypertension among US adults? Am J Hypertens 2008;21:159–65.
22. Wong TY, Hyman L. Population-based studies in ophthalmology. Am J Ophthalmol 2008;146:656–63.
23. ARIC Investigators. The Atherosclerosis Risk in Communities (ARIC) Study: design and objectives. Am J Epidemiol 1989; 129:687–702.
24. Xu L, Cui T, Zhang S, et al. Prevalence and risk factors of lens opacities in urban and rural Chinese in Beijing. Ophthalmology 2006;113:747–55.

25. Mitchell P, Smith W, Attebo K, Wang JJ. Prevalence of age-related maculopathy in Australia: the Blue Mountains Eye Study. Ophthalmology 1995;102:1450–60.
26. Fried LP, Borhani NO, Enright P, et al. The Cardiovascular Health Study: design and rationale. Ann Epidemiol 1991;1: 263–76.
27. Augood C, Fletcher A, Bentham G, et al. Methods for a population-based study of the prevalence of and risk factors for age-related maculopathy and macular degeneration in elderly European populations: the EUREYE Study. Ophthalmic Epidemiol 2004;11:117–29.
28. Kawasaki R, Wang JJ, Rochtchina E, et al. Cardiovascular risk factors and retinal microvascular signs in an adult Japanese population: the Funagata Study. Ophthalmology 2006;113: 1378–84.
29. Liang YB, Friedman DS, Wong TY, et al, Handan Eye Study Group. Prevalence and causes of low vision and blindness in a rural Chinese adult population: the Handan Eye Study. Ophthalmology 2008;115:1965–72.
30. Wang FH, Liang YB, Zhang F, et al. Prevalence of diabetic retinopathy in rural China: the Handan Eye Study. Ophthalmology 2009;116:461–7.
31. Oshima Y, Ishibashi T, Murata T, et al. Prevalence of age related maculopathy in a representative Japanese population: the Hisayama study. Br J Ophthalmol 2001;85:1153–7.
32. Varma R, Paz SH, Azen SP, et al, Los Angeles Latino Eye Study Group. The Los Angeles Latino Eye Study: design, methods, and baseline data. Ophthalmology 2004;111: 1121–31.
33. Klein R, Klein BE, Knudtson MD, et al. Prevalence of age-related macular degeneration in 4 racial/ethnic groups in the multi-ethnic study of atherosclerosis. Ophthalmology 2006; 113:373–80.
34. West SK, Klein R, Rodriguez J, et al. Diabetes and diabetic retinopathy in a Mexican-American population: Proyecto VER. Diabetes Care 2001;24:1204–9.
35. Hofman A, Breteler MM, van Duijn CM, et al. The Rotterdam Study: objectives and design update. Eur J Epidemiol 2007; 22:819–29.
36. van Leeuwen R, Klaver CC, Vingerling JR, et al. The risk and natural course of age-related maculopathy: follow-up at 6 1/2 years in the Rotterdam study. Arch Ophthalmol 2003;121: 519–26.
37. Chen SJ, Cheng CY, Peng KL, et al. Prevalence and associated risk factors of age-related macular degeneration in an elderly Chinese population in Taiwan: the Shihpai Eye Study. Invest Ophthalmol Vis Sci 2008;49:3126–33.
38. Foong AW, Saw SM, Loo JL, et al. Rationale and methodology for a population-based study of eye diseases in Malay people: the Singapore Malay Eye Study (SiMES). Ophthalmic Epidemiol 2007;14:25–35.

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[1] Centre for Eye Research Australia, University of Melbourne, Royal Victorian Eye and Ear Hospital, VIC, Australia.

[2] Centre for Vision Research, University of Sydney, NSW, Australia.

[3] Allergan, Inc, Irvine, California.

[4] Singapore Eye Research Institute, National University of Singapore, Singapore.

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Correspondence:
Tien Y. Wong, MD, PhD, Centre for Eye Research Australia, University of Melbourne, 32 Gisborne Street, East Melbourne 3002, Australia. E-mail: twong@unimelb.edu.au.

Appendix 1. The International Eye Disease Consortium

Sophie Rogers, Rachel L. McIntosh, Ning Cheung, Lyndell Lim, Jie Jin Wang, Paul Mitchell, Ronald Klein, Barbara E. K. Klein, Liang Xu, Jost Jonas, Usha Chakravarthy, Astrid Fletcher, Ryo Kawasaki, Hidetoshi Yamashita, Takamasa Kayama, Ningli Wang, Yuanbo Liang, Miho Miyazaki-Yasuda, Tatsuro Ishibashi, Yutaka Kiyohara, Rohit Varma, Mary Frances Cotch, Sheila West, Beatriz Munoz, Johannes Vingerling, Lintje Ho, Paulus de Jong, Ching-Yu Cheng, Shih-Jen Chen, Seang Mei Saw, Tin Aung, Jonathan W. Kowalski, Hiep P. Nguyen, and Tien Y. Wong.

シンポジウム

3. 糖尿病の血管合併症のトータルケア：早期診断，そして予防へ
3）糖尿病網膜症

石橋　達朗　　安田　美穂

Key words：空腹時血糖値，糖負荷後2時間血糖値，HbA_{1C}，糖尿病罹病期間

はじめに

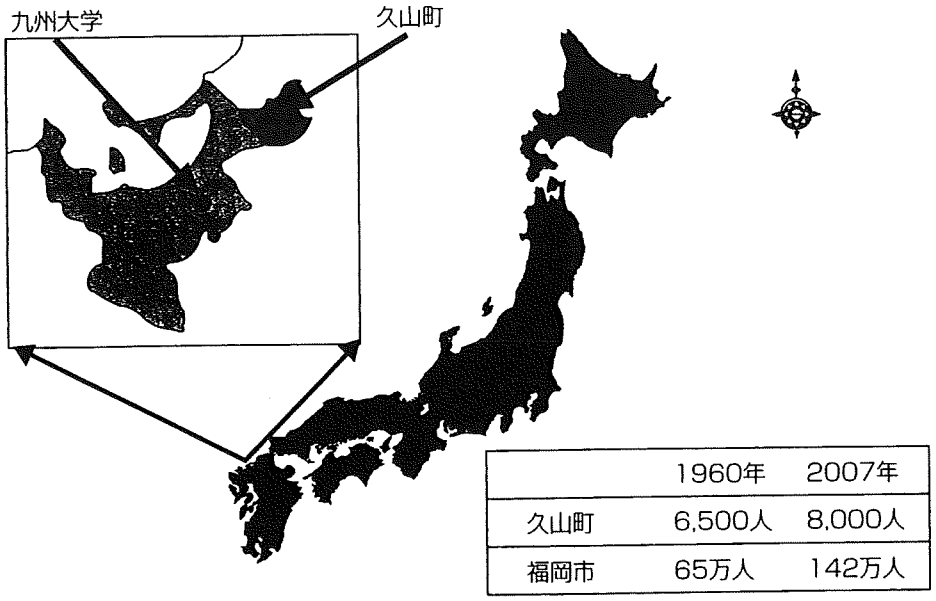
糖尿病網膜症（網膜症）は糖尿病の代表的な合併症である．厚生労働省による2007年の糖尿病実態調査ではわが国における糖尿病患者総数は890万人と報告されている．現在も糖尿病自体の患者数はさらに増加しつつあり，今後もその傾向は変わらないと予想されている．これに伴い網膜症患者数も増加することが容易に想像できる．網膜症において最も重要な点は神経網膜が病変の主座であり，一旦障害されると現在の最善の治療を施しても視機能の回復は困難なことである．再生医療が注目される今日ではあるが，実用化にはもう少し時間がかかりそうである．現時点において最善の治療は予防であり，むしろ予防医学は今後さらに重要視されるであろうし，各個人にカスタマイズされた医療がより具体的に臨床の現場に入り込んでくるものと予測される．網膜症に対する予防的治療の確立のためには，糖尿病ならびに合併症の有無を把握し，長期にわたり追跡していくことが重要である．

福岡県久山町は福岡市東部に隣接する人口約7,500人の都市近郊型農村地域で，人口の年齢分布や職業構成および生活様式や疾病構造（高血圧，高脂血症，肥満，糖尿病など）が全国統計と差異がなく，わが国の平均的な集団であるとされている（図1～3）．1998年より九州大学眼科では福岡県久山町における住民健診に参加し，その後約10年間にわたり2,000人以上におよぶ住民を対象にプロスペクティブな追跡調査を行ってきた．平成19年には，データの精度を上げるため久山町全住民へ眼科健診への参加を促し，70%以上の受診率を得ることができた．大規模な眼科健診を長期的に行うことにより，日本で初めての大規模な眼科疫学研究が可能となり，網膜症の危険因子・防御因子および疾患と生活習慣や環境要因との関係が明らかになってきた．また，今までの調査結果を欧米の結果と比較することにより日本人での網膜症発症の特徴が明らかになってきた．この疫学調査の結果から，わが国の網膜症の疫学について概説する．

1．網膜症有病率

これまで，わが国においては網膜症の疫学研究，特に住民を対象としたpopulation-based studyはあまり行われていない．実際の網膜症の患者数を把握するために我々は久山町での疫学研究を開始した．1998年に40歳以上の久山町全住民を対象に糖尿病および網膜症の有病率の調

いしばし　たつろう，やすだ　みほ：九州大学大学院医学研究院眼科学分野



	1960年	2007年
久山町	6,500人	8,000人
福岡市	65万人	142万人

図 1. 久山町と人口推移

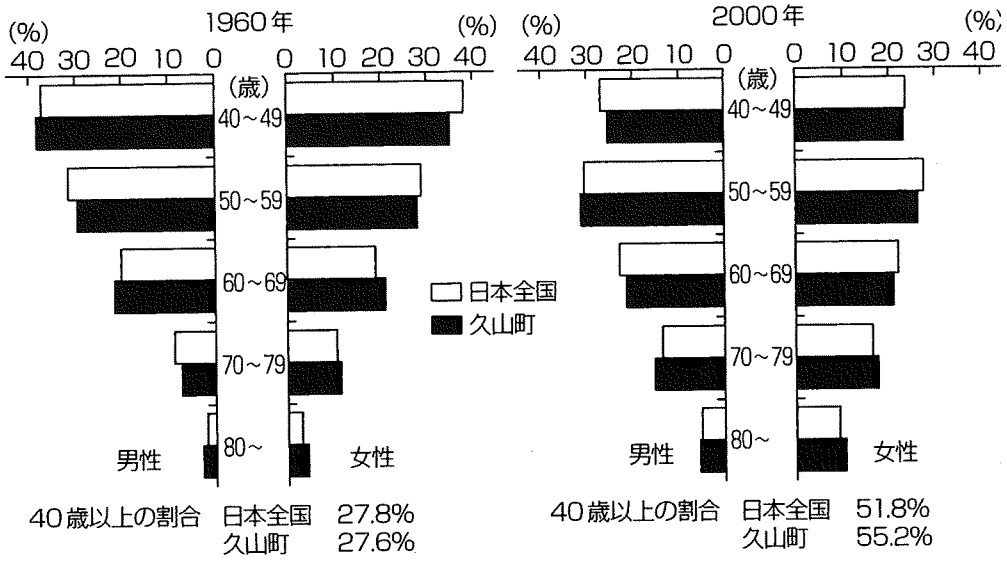


図 2. 久山町と全国の年齢階級別人口構成の比較

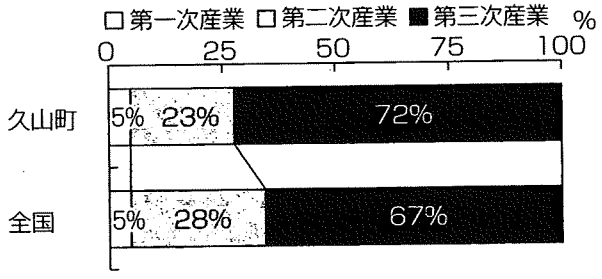


図 3. 久山町と全国の就労人口の産業別割合

査を開始し，糖尿病の有病率は 16.3%，網膜症の有病率は 2.6%（糖尿病患者の 15.8%）であることがわかった（図 4）．この結果をわが国の 40 歳以上の総人口に換算すると，網膜症患者数は 1998 年では 166 万人と推定される．

2. 網膜症発症の危険因子

新たに網膜症を発症する危険因子は何であるのかについて追跡調査を行ってきた．具体的には 1998 年の久山町眼科健診受診者をベースラインのコホート集団に設定し，2007 年の久山町眼

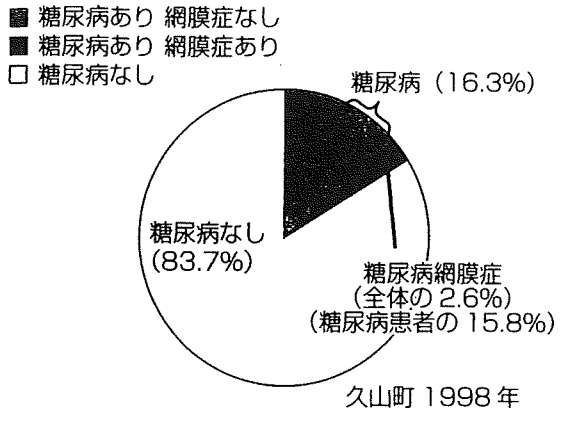


図 4. 糖尿病網膜症の有病率(久山町　1998 年)

科健診でベースラインのコホート集団を追跡する 9 年間の前向きコホート調査を行った．1998 年に住民健診を受けた福岡県久山町在住の 40～79 歳の住民 1,637 名のうち，網膜症の既発症者 37 名を除いた 1,600 名を 5 年間追跡し，2007 年に再度住民健診を受けた 1,347 名を追跡した．発症に関係する危険因子を調査するために，年齢，性別，HbA_{1c}，糖尿病罹病期間，高血圧，高脂血症，喫煙，飲酒，Body Mass Index，白血球数の 10 の因子のうち，5 年後の網膜症発症に有意に関連している因子を探索した．その結果，糖尿病罹病期間と$ヘモグロビンA_{1c}$が網膜症発症の有意な危険因子となった（表 1）．糖尿病の罹病期間 5 年未満をオッズ比 1.0 とすると，5 年から 10 年でリスクは有意に増加し，オッズ比 5.1，さらに 10 年以上ではオッズ比 9.0 とそのリスクは急増した．この結果から，糖尿病罹病期間が長くなると，網膜症の発症に注意する必要があることがわかった．また，$ヘモグロビンA_{1c}$7.0% 以下をオッズ比 1.0 とすると，7.0 から 8.0% でそのリスクは有意に増加し，オッズ比 6.7，8.0% 以上ではオッズ比 30.7 とリスクが大きく増加した．この結果から，長期にわたり網膜症の発症を予防するためには，$ヘモグロビンA_{1c}$を 7.0% 以下に抑える必要があることがわかった．つまり$ヘモグロビンA_{1c}$を低めに維持することが網膜症の発症に最も重要であり，とくに罹患期間が長い糖尿病患者においては血糖管理を厳しくおこなうことが重要である．

3. 糖尿病の診断基準

1997 年に ADA（American Diabetes Association），1998 年に WHO（World Health Organization）が糖尿病の新しい診断基準を示した[1]．すなわち空腹時血糖値が 126 mg/dl 以上または糖負荷後 2 時間血糖値が 200 mg/dl 以上と決定された．これらの診断基準は欧米の population-based study での血糖値レベルと網膜症の関係から算出されたものである．日本では一般住民を対象に血糖値レベルと網膜症の関係を調査した研究はなく，欧米での診断基準に基づいて糖尿病の診断基準が決められている．日本人と欧米人では人種はもちろん体格や食事内容も違うため欧米での診断基準をそのまま日本人にあてはめるのは適当ではない．そこで日本人において，糖尿病を診断するための空腹時血糖値，2 時間血糖値，HbA_{1c}値のそれぞれの診断基準値を決定するために，1998 年久山町住民健診で経口血糖負荷試験および眼科健診を受けた 40～79 歳の男女 1,637 名を対象として網膜症有病率を算出し，それぞれの測定値について最適な診断基準値を決定した[2]．具体的にはそれぞれの測定値の 10 分位による網膜症有病率を算出し，さらに ROC（receiver operating characteristic）曲線から敏感度（Sensitivity）と特異度（Specificity）が最大となる空腹時血糖値，2 時間血糖値を算出して最適な診断基準値を決定した．その結果，空腹時血糖値，2 時間血糖値，HbA_{1c}値の 10 分位による網膜症有病率はそれぞれ 117 mg，200 mg，5.8% から著明に増加した（図 5）．また ROC 曲線を用いて敏感度および特異度が最大となるそれぞれの最適な診断基準値を算出すると，空腹時血糖値が 116 mg，2 時間血糖値が 200 mg となり，10 分位値ともほぼ一致した（表 2）．この結果から日本人では，空腹時血糖値が 116 mg，2 時間血糖値が 200 mg のところに cut-off point があり，2 時間

表1. 糖尿病網膜症発症の危険因子（久山町　1998～2007年）

危険因子	年齢，性調整		多変量調整	
	OR	(95%CI)	OR	(95%CI)
糖尿病罹病期間（年）	1.15**	(1.11～1.19)	1.10*	(1.06～1.15)
$HgbA_{1c}$ (%)	2.40**	(1.90～3.04)	1.90**	(1.46～2.47)
高血圧	1.21	(0.62～2.36)		
BMI (kg/m^2)	0.97	(0.88～1.07)		
総コレステロール（mmol/l）	1.08	(0.76～1.53)		
HDLコレステロール（mmol/l）	0.20	(0.03～1.20)		
中性脂肪（g/l）	0.81	(0.54～1.20)		
喫煙	0.90	(0.38～2.11)		
飲酒	0.92	(0.44～1.91)		

OR：オッズ比，CI：信頼区間，**$p<0.01$，*$p<0.05$

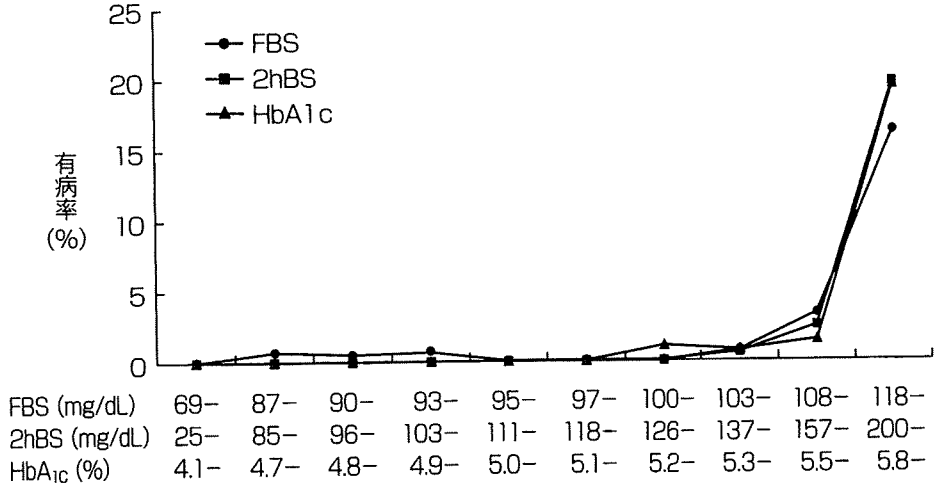


図5. 血糖値，HbA_{1c}10分位別に見た糖尿病網膜症の有病率（久山町　1998年）

表2. 糖尿病診断基準値の最適値（久山町　1998年）

	空腹時血糖値	2時間血糖値
最適値	116 mg/dl	200 mg/dl
敏感度（%）	86.5	86.5
特異度（%）	87.3	89.6

血糖値は現在の診断基準値と一致するが，空腹時血糖値は現在の診断基準値よりも低いレベルから網膜症の合併症が出現していることがわかった．これらの結果をもとに今後日本人における糖尿病の診断基準を見直す必要があると思われる．

文　献

1) Harris MI, et al : Comparison of diabetes diagnostic categories in the U.S. population according to the 1997 American Diabetes Association and 1980-1985 World Health Organization diagnostic criteria. Diabetes Care 22 : 1859–1862, 1997.
2) Miyazaki M, et al : Comparison of diagnostic methods for diabetes mellitus based on prevalence of retinopathy in a Japanese population : the Hisayama Study. Diabetologia 47 : 1411–1415, 2004.

あたらしい眼科 26(1)：25～30，2009

観察研究（コホート研究）：久山町スタディ

Observational Study (Cohort Study)：The Hisayama Study

安田美穂*

はじめに

Evidence-based medicine（EBM）が求められるなか，わが国独自のエビデンスは少ない．しかし九州大学病態機能内科学を中心に福岡県久山町で1961年から進められている「久山町スタディ」は，日本においても世界の水準をゆく大規模な前向きコホート研究であり，その臨床疫学研究データはわが国独自のエビデンスとなっている．久山町の長期疫学研究は40年以上もの間，久山町当局・住民と良好な信頼関係を築き，常に40歳以上の住民の8割以上を検診し，徹底した追跡調査（追跡率99%）を行うとともに全町死亡例の8割以上を剖検して死因を明らかにするなど，世界でも類をみない精度で多種多様な臨床記録を収集してきている．この研究の全貌を知ることは，疫学研究のあり方やわが国独自の臨床医学のあり方を検討するうえで意義深いと思われる．

そもそも久山町スタディが始まったきっかけはわが国の死亡統計の信憑性に疑問が投げかけられたことに始まる．1953～1957年の脳血管疾患死亡率は日本で欧米諸国の約2倍の高率を示し，かつ脳出血の比率は約10倍以上と圧倒的に多く脳出血で死亡していた．このことについて，米国の疫学者は日本人医師の診断習慣と能力に疑問を投げかけたが，これに科学的に反論できる国内データがなかった．この疑問を解明するために，特定の地域住民を対象に，その集団内の脳卒中死亡・発症を正確にとらえた疫学研究が立案され，同時に発症要因を明らかにすることにより，疾病の予防につなげようと始められたのが久山町スタディである．

I　久山町とは

複数の候補地のなかから，福岡市東部に隣接する久山町（図1）が選ばれた理由はいくつかある．研究開始時の1961年当時，久山町の人口は約6,500人の都市近郊型の農村地域で，①対象とした40歳以上の町人口の年齢分布，職業構成が日本全体の平均に近似していること，②人口の流出入が年平均5%以内と小さいこと（町の96%が市街化調整区域に指定），③九州大学に近く，住民の検診，往診体制がとれること，そして④町当局と住民の理解と全面的な協力が得られることなどがあげられる[1]．

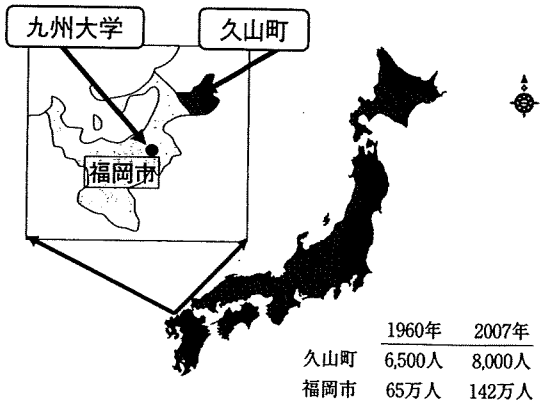


図1　久山町と人口推移（あたらしい眼科 **24**：1278-1290，2004より改変）

*Miho Yasuda：九州大学大学院医学研究院眼科学分野 久山町研究室
〔別刷請求先〕安田美穂：〒811-2501 福岡県糟屋郡久山町大字久原1822-1 ヘルスC＆Cセンター内　九州大学久山町研究室

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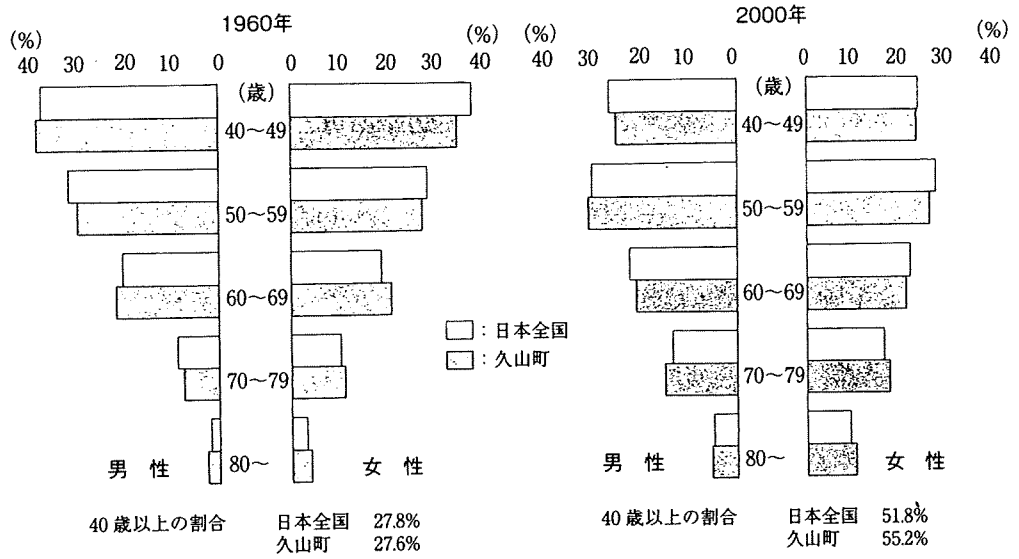

図 2　久山町と全国の年齢階級別人口構成の比較（あたらしい眼科 **24**：1278-1290，2004 より）

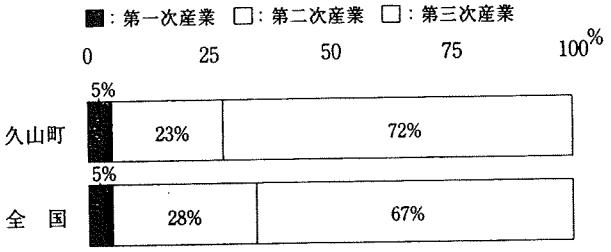

図 3　久山町と全国の就労人口の産業別割合（あたらしい眼科 **24**：1278-1290，2004 より）

1961 年開始時の 40 歳以上の対象人口は全人口 6,521 名の 27.6% を占め，全国の 27.8% と変わらず，年齢分布も近似している．職業構成は農林業の第一次産業従事者が 5%，第二次産業（工業）が 23%，第三次産業（サービス業）が 72% と全国のそれ（5%，28%，67%）と基本的には変わらない（図 2, 3）．ほかに生活様式，疾病構造（高血圧，高脂血症，肥満，糖尿病など）は各時代とともに全国統計と差異がなく，久山町はわが国の平均的な集団であり，普遍性に富んでいる．人口は 40 年間に 1,000 人増えたにすぎず，移動の少ない町である．

II　久山町スタディの特徴

久山町スタディは 1961 年の成人健診を皮切りに始まり，研究の基本的スタイルは脳卒中をはじめとする心血管病の前向き追跡研究である．最近ではその研究対象疾患は脳血管障害，虚血性心疾患，腎疾患，悪性腫瘍，老年期痴呆，肝疾患からその危険因子である高血圧，糖尿病，高脂血症，肥満，栄養，運動，飲酒，喫煙などに及んでおり，久山町の住民は生活習慣を長期にわたり包括的に検討できるわが国で唯一の集団といえる．九州大学眼科学分野ではこれに 1998 年から本格的に参画し，40 歳以上の住民を対象に大規模な健診データに基づく眼科疾患の疫学調査を現在進行中である．久山町スタディに参画し大規模な眼科健診を長期的に行うことにより，前向きの眼科疫学研究（コホート研究）が可能となり，包括的な健診成績のなかより種々の眼科疾患の危険因子，防御因子および疾患と生活習慣や環境要因との関係を明らかにすることができる．

III　久山町スタディのしくみ

久山町スタディでは 1 年に一度の通常健診と 5 年ごとの大健診を行っている．眼科健診もこれに従って，1 年に一度の通常健診と 5 年ごとの大健診を行っている．通常健診での眼科健診項目は，眼圧，眼底写真（無散瞳）の 2 項目で，大健診時の健診項目は，屈折，眼圧，眼軸長，網膜厚（光干渉断層計：OCT），眼底写真（散瞳），細隙灯検査（散瞳），眼底検査（散瞳）の 7 項目を基本としているが，健診年次により項目の追加や削除を行って