Prevalence of Early and Late Age-Related Macular Degeneration in India: The INDEYE Study

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Purpose. To estimate the prevalence of early and late age-related macular degeneration (AMD) in India.

Methods. Of 7518 people aged 60 years and older identified from randomly sampled villages in North and South India, 5853 (78%) attended an eye examination including fundus photography. Fundus images were graded according to the Wisconsin Age-Related Maculopathy Grading System.

Results. Fundus images were ungradable in 1587 people, mainly because of cataract. People 80 years of age and older were less likely to attend the eye examination and more likely to have ungradable images. For ages 60 to 79 years, the percent prevalence (95% confidence interval [CI]) were late AMD 1.2 (0.8–1.5); and early AMD: grade 1 (soft distinct drusen or pigmentary irregularities), 39.3 (37.2–41.5); grade 2 (soft distinct drusen with pigmentary irregularities or soft indistinct or reticular drusen), 6.7 (5.8–7.6); and grade 3 (soft indistinct or reticular drusen with pigmentary irregularities), 0.2 (0.1–0.4). For ages 80 and older, the respective percent prevalence was: late AMD, 2.5 (0.4–4.7); and early AMD: grade 1, 43.1(35.7–50.6); grade 2, 8.1 (4.3–12.0); and grade 3, 0.5 (0–1.5).

Conclusions. The prevalence of early AMD (grades 1 and 2) is similar to that observed in Western populations, but grade 3 appears to be lower. The prevalence of late AMD is comparable to that in Western populations in the age group 60 to 79 years. It is likely that the prevalence in the 80 and older age group is underestimated. (*Invest Ophthalmol Vis Sci.* 2010;51: 701–707) DOI:10.1167/iovs.09-4114

Evidence is now emerging from different population settings of the prevalence of age-related macular degeneration (late AMD). Differences in prevalence from diverse populations may offer insights into possible environmental and genetic causes of AMD. Comparison of prevalence rates across studies is critically dependent on the age of the populations recruited. Age-specific prevalence rates allow for more meaningful comparisons, but in many studies the number of people in the oldest age groups (75 years and older or 80 years and older) was very small, resulting in uncertainty in the prevalence estimates. Most studies specifically designed to investigate the prevalence of AMD have been undertaken in Western populations among people of European origin.[1–6] These studies have reported relatively consistent age-specific prevalence estimates of AMD of ~4% of those aged 70 to 79 and 12% of those aged 80 and older,[7] with the exception of the Reykjavik study,[6] which reported twofold higher rates among those aged 80 and older. Data on other ethnic groups in Western countries are more scarce, although studies suggest substantially lower rates in African Americans[8–10] compared with Europeans and inconsistent results for Hispanic Americans.[9,11–13] There are at present no data from studies in either Africa or Latin America. The Barbados study in an African Caribbean population also found a lower prevalence of late AMD[14] than did studies in Europeans or those of European origin. Studies in Asia have reported mixed results, with a low prevalence of AMD in the Beijing Eye Study[15] and the Hisayama Study in Japan[16] and a prevalence similar to that of Europeans in the Shiphai study, Taiwan,[17] and possibly in the Singapore Malay Study[18] and Funagata Study in Japan.[19] As one study excluded people aged 80 and older,[18] and two others excluded people with chronic health problems,[16,19] these studies were based on small numbers of older people and cases of late AMD with potential bias in the types of older people included. Three studies in India reported prevalence rates in the 70 and older age group of 2%,[20] 3.7%,[21] and 4.6%,[22] but the number of people in the age group 70 and older was low (~300 in each study). One of these studies was the INDEYE feasibility study,[22] which was undertaken to provide estimates of late AMD for determining the sample size for the present two-center study (INDEYE) We report the results of the prevalence of early and late AMD in the INDEYE study.

Methods

The INDEYE study is a population-based study of people aged 60 years and older. The objectives of the INDEYE study were to estimate the age- and sex-specific prevalence of early and late AMD and of lens opacities, and to investigate associations of these conditions with tobacco use, exposure to biomass cooking fuels, outdoor work, and dietary factors. In this article we report the results of a determination of the prevalence of AMD. The study took place in two locations: the Gurgaon district, in Haryana state, North India, and the Pondicherry union territory and Cuddalore district in Tamil Nadu, South India. These areas were chosen to represent a mix of rural and urban populations served by the participating eye hospitals (Dr. Rajendra Prasad

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Centre [RPC]), Delhi; the All India Institute of Medical Sciences, Delhi; and the Aravind Eye Hospital [AEH], Pondicherry). A total of 59 clusters, 29 in North India, and 30 in South India were randomly selected on the basis that 8% of the total population would be aged 60 years and older. In this study, we sought to enroll 3000 people aged 60 years and older in each of the two study centers, allowing for a response rate of ~80%. The sample size calculations were based on an estimated prevalence of late AMD of 3.0% with 90% confidence and a precision of ±0.4% and a design effect of 1.2. These assumptions were based on the results from the INDEYE feasibility study of people 60 and older.

Before the start of the study, meetings were held with local village leaders to explain the study objectives and methods. A total of 7518 people 60 years of age and older (3586 in North India and 3932 in South India), were identified from enumeration and invited to take part in the study. Recruitment into the study was performed between 2005 and 2007. Informed written consent was obtained from all participants before enrollment. Information was read to people who were illiterate in the presence of a local witness, and a thumb impression of the participant signified assent. The study complied with the guidelines in the Declaration of Helsinki, and ethics approval was received from the Research Ethics Committees of the All India Institute of Medical Sciences, Aravind Eye Hospital, London School of Hygiene and Tropical Medicine, Queens University Belfast, and the Indian Council for Medical Research.

Study Procedures

Information on household characteristics and sociodemographic variables was collected at enumeration. Participants were interviewed at home by trained fieldworkers who used a structured questionnaire that inquired about tobacco and alcohol use, cooking fuels and practices, and outdoor work. Diet was assessed by 24-hour recall. Within a week of the home interview participants were brought to the base hospital for the clinical examination which included anthropometry, blood pressure, an eye examination, and blood sample collection for antioxidant analysis.

Eye Examination

Visual acuity (VA) was tested with the tumbling E ETDRS chart and recorded in each eye separately with the subject wearing habitual spectacles (if any). If VA in either of the eyes of a participant was worse than logMAR 0.6, refraction was performed with an autorefractor (Nikon, Tokyo, Japan), and best corrected acuity was recorded. Pupillary dilation was achieved with 1% tropicamide after anterior segment biomicroscopy. A clinical examination of each eye was performed that included anterior and posterior segment assessments, using slit lamp biomicroscopy. Digital images of the lens were taken by digital photo slit lamp for nuclear opacities (model SL-D7; Topcon, Tokyo, Japan) and with a camera for cortical and posterior subcapsular opacities (Neitz Instruments Co., Ltd., Tokyo, Japan). Lens opacities were graded according to the Lens Opacities Classification System III (LOCS III). Fundus photography was undertaken with a fundus acquisition system (TRC 50 EX; Topcon) with preinstalled software (IMAGEnet; Topcon) and a high-resolution camera (Nikon). Two 35° stereo photographs of standard field 2 (based on the Wisconsin Age-Related Maculopathy Grading System) were obtained from each eye. The images were saved to compact disks and mailed to the grading center (Department of Ophthalmology and Vision Science, Queens University Belfast). The study protocol also required that fundus images also be taken after cataract surgery for those participants recommended for surgery: one within 24 hours of surgery (first postsurgical day) and the next, 4 to 6 weeks after surgery when the patient attended for the postoperative checkup.

Grading of Images

Grading of age-related macular degeneration was based on the Wisconsin Age-Related Maculopathy Grading System (WARMGS)[23] and performed by two experienced graders adjudicated by a senior grader and the reading center clinician. Graders in the reading center of the Queen's University of Belfast participated in concordance and quality control exercises and training programs, with input and accreditation from the University of Wisconsin Fundus Photographic and Angiographic Reading Center. Features of early AMD were classified into five mutually exclusive grades : grade 0 (no early or late AMD); grade 1, soft distinct drusen (≥63 μm) only *or* pigmentary irregularities only; grade 2, soft indistinct (≥125 μm) or reticular drusen only *or* soft distinct drusen (≥ 63 μm) with pigmentary irregularities; grade 3, soft indistinct (≥125 μm) or reticular drusen with pigmentary irregularities; grade 4, either choroidal neovascularization (CNV; presence of any of the following: serous or hemorrhagic retinal or retinal pigment epithelial detachment, subretinal neovascular membrane, and periretinal fibrous scar) or geographic atrophy (GA; well-demarcated area of retinal pigment atrophy with visible choroidal vessels). This grading system was validated in the Rotterdam Eye Study.[24] Early AMD was defined as grades 1 to 3 and late AMD as grade 4. All questionable lesions and all eyes classified as having late AMD were adjudicated by a reading center clinician. Any lesions considered to be due to other causes such as myopia and inflammatory disease were excluded. When CNV and GA were both present in the same eye, we classified the eye as CNV, as it is not possible to determine whether the GA was a primary phenomenon or secondary to the neovascular process.

Statistical Analysis

Statistical analysis was performed with commercial software (Stata 10; 2007 Stata Statistical Software; StataCorp LP, College Station, TX). Principal component analysis was used to derive a socioeconomic status index (SES) (caste, landholding, type of roof, and number of rooms in the house, excluding the kitchen, toilets, and bathrooms). A summary variable on tobacco use was based on responses to tobacco smoking (bidi and/or cigarettes), chewing, or inhaling. Body mass index (BMI; weight in kilograms/height in meters squared) was categorized according to World Health Organization guidelines.[25] Differences between examination attendees and nonattendees and between those with gradable or nongradable fundus images were tested by design-adjusted Wald tests and multivariable logistic regression. The overall age- and sex-specific prevalence (%) of early and late AMD was calculated for each center, excluding people with ungradable images. Age and sex standardization using the total study population as the standard (direct standardization) was performed to estimate the prevalence of early and late AMD by center. Poisson regression was used to examine the association of age and sex with the prevalence of early and late AMD. To take account of missing information we used binomial general linear regression models to estimate the prevalence of late AMD in the enumerated population and in those with ungradable fundus images with covariates associated with late AMD and with either nonattendance or ungradable fundus images. All analyses took account of the sampling design in the estimation of robust standard errors and corresponding probabilities and 95% confidence intervals (CIs).

Results

A total of 7518 people of age 60 years and older were enumerated and, of those, 5900 (78.5% response rate) attended a hospital-based eye examination (Fig. 1). The response rate to the clinical examination was similar in the two study centers (79% North India, 78% South India). In both centers, older people (aged 75 and older) were less likely to attend, but there were no differences between attendees and nonattendees in sex, landholding, or caste, nor, in the South, in education (Table 1). There was a small difference in the North in education, with people with lower levels of education being slightly more likely to be examination nonattendees. Of the 5900 people who attended the eye examination, 5853 underwent fundus photography, of which 1847 did not have gradable images at the first examination. In nearly a one fourth of those (n = 421), fundus images that were acquired after cataract

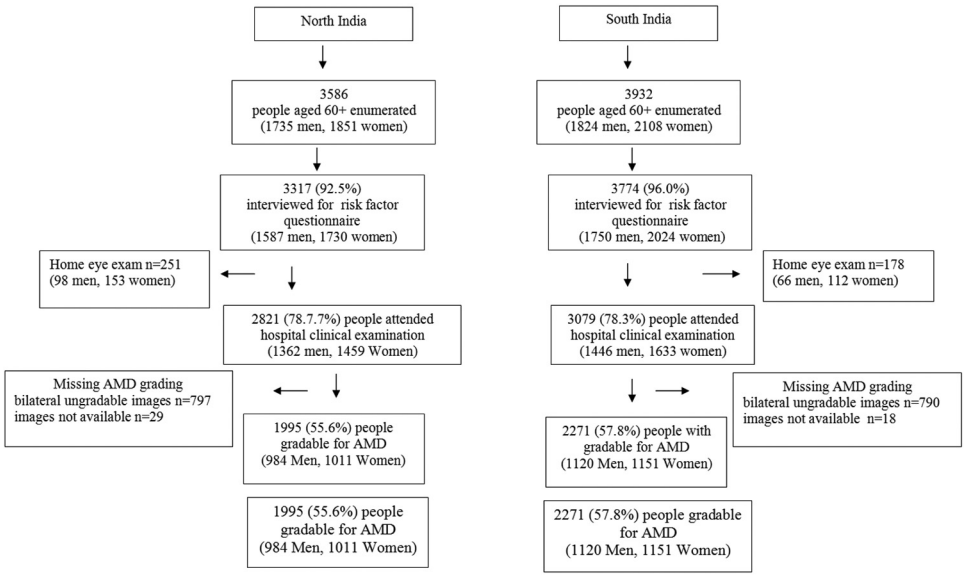

FIGURE 1. Study flow chart.

surgery were gradable in 260 persons and remained ungradable in 161. In total, 4266 people had at least one gradable image, and 1587 had images that could not be graded in either eye. The proportion of people with bilateral ungradable images was similar in both centers: 28.6% (797/2792) in North India and 25.8% in South India (790/3061). The main reason for bilateral ungradable images was cataract (85%). Eleven percent of people with ungradable images ($n = 175$) had a history of bilateral cataract surgery. In this group of people, the principal reasons for poor images included postsurgical capsular opacification (30%, $n = 53$), inability to achieve adequate dilation (18%, $n = 32$), and corneal opacities (17%, $n = 29$). Of all with bilateral ungradable images, 1397 (88.1%) were bilaterally vision impaired (VA <6/18), and 404 (25.4%) were bilaterally blind (VA <3/60), based on presenting vision in the better eye. In the multivariate analysis, compared with those with gradable fundus images, persons who had ungradable images were older and were more likely to be women, members of the

TABLE 1. Characteristics of Clinical Examination Attendees and Nonattendees by Study Center

	North India			South India		
Characteristics *n* (%)	**Clinical Exam Attendees (*n* = 2821)**	**Clinical Exam Nonattendees (*n* = 765)**	***P****	**Clinical Exam Attendees (*n* = 3079)**	**Clinical Exam Nonattendees (*n* = 853)**	***P****
Men	1362 (48.3)	373 (48.8)	0.8	1446 (47.0)	378 (44.3)	0.2
Age group, y						
60–64	1032 (36.6)	226 (29.5)	<0.0001	1112 (36.1)	248 (29.1)	<0.0001
65–69	700 (24.8)	166 (21.7)		899 (29.2)	213 (25.0)	
70–74	579 (20.5)	140 (18.3)		596 (19.4)	180 (21.1)	
75–79	305 (10.8)	95 (12.4)		287 (9.3)	104 (12.2)	
80+	205 (7.3)	138 (18.0)		185 (6.0)	108 (12.7)	
Area						
Urban	297 (10.5)	95 (12.4)	0.3	1246 (40.5)	369 (43.3)	0.1
Rural	2524 (89.5)	670 (87.6)		1833 (59.5)	484 (56.7)	
Marital status						
Currently married	1863 (66.0)	462 (60.4)	<0.01	1754 (57.0)	447 (52.4)	<0.04
Widow/widower	916 (32.5)	290 (37.9)		1247 (40.5)	388 (45.5)	
Land holdings						
No land holdings	1288 (45.7)	353 (46.1)	0.9	2586 (84.0)	710 (83.2)	0.1
>0 to <10 acres land	1418 (50.3)	412 (53.9)		455 (14.8)	120 (14.1)	
≥10 acres land	115 (4.1)	29 (3.8)		38 (1.2)	23 (2.7)	
Schedule caste	520 (18.4)	149 (19.5)	0.5	605 (19.7)	196 (23.0)	0.1
Education						
Higher†	59 (2.1)	7 (0.9)	<0.05	106 (3.4)	35 (4.1)	0.5
10–13 y school	243 (8.6)	62 (8.1)		361 (11.7)	90 (10.6)	
1–9 y school	440 (15.6)	132 (17.3)		861 (28.0)	243 (28.5)	
Illiterate	2023 (71.7)	564 (73.7)		1660 (53.9)	485 (56.9)	
Lowest SES‡	619 (21.9)	175 (22.9)	0.6	692 (22.5)	193 (22.6)	0.9

* *P* for difference between attenders and nonattenders.
† Diploma, graduate, post graduate or professional education.
‡ Socioeconomic index ranging from 1 (lowest) to 5 (highest).

TABLE 2. Multivariable Logistic Regression* of Characteristics Associated with Ungradable Images

Characteristics *n* (%)	Gradable Images† (*n* = 4266)	Ungradable Images† (*n* = 1587)	Odds Ratio (95% CI)	*P*
Men	2104 (49.3)	683 (43.0)	1	<0.01
Women	2162 (50.7)	904 (57.0)	1.3 (1.1–1.5)	
Age group, y				
60–64	1763 (41.3)	372 (23.4)	1	<0.0001
65–69	1207 (28.3)	381 (24.0)	1.5 (1.3–1.8)	
70–74	760 (17.8)	405 (25.5)	2.5 (2.0–2.9)	
75–79	339 (8.0)	249 (15.7)	3.7 (3.0–4.5)	
80+	197 (4.6)	180 (11.3)	4.5 (3.6–5.7)	
Schedule caste	705 (16.5)	412 (26.0)	1.6 (1.2–2.0)	<0.001
Illiterate	2444 (57.3)	1202 (75.7)	1.1 (1.0–1.2)	<0.001
Lowest SES‡	859 (20.1)	436 (27.5)	0.9 (0.8–1.2)	0.9
Tobacco use				
Never	1693 (39.7)	527 (33.2)	1	
Past	764 (9.9)	236 (8.3)	0.9 (0.7–1.1)	0.3
Current	2149 (50.4)	929 (58.5)	1.1 (0.9–1.3)	0.1
BMI				
Normal weight (18.5–<25.0)	2258 (53.1)	766 (48.9)	1	
Underweight (<18.5)	1217 (28.6)	634 (40.4)	1.3 (1.2–1.5)	<0.001
Overweight (≥25.0)	778 (18.3)	167 (10.7)	0.8 (0.6–0.9)	<0.05

* Adjusted for all variables in the table.
† Data shown are *n* (%).
‡ Socio-economic index ranging from 1 (lowest) to 5 (highest).

lowest caste group (schedule caste), illiterate, and underweight. There was no difference in the prevalence of tobacco use or being in the lowest SES group (Table 2).

Of those with gradable images, nearly 40% in both centers had signs of grade 1 AMD (Table 3). The age- and sex-standardized prevalence of grade 2 AMD was 5.4% (95% CI, 4.4–6.4) in North India and 8.0% (95% CI, 6.9–9.1) in South India ($P < 0.01$) There was only one person in North India with grade 3 AMD (0.05%; 95% CI, 0–0.10) and 10 persons in South India (0.4%; 95% CI, 0.2–0.7; $P < 0.05$). The prevalence of late AMD (grade 4) was very similar in both centers: 1.2% (95% CI, 0.7–1.6) in North India and 1.3% (95% CI, 0.9–1.8) in South India—a combined prevalence of 1.2 (95% CI, 0.9–1.6). The prevalence of late AMD increased from 60 to 64 years to 75 to 79 years, but there was no further increase in prevalence at 80 years and older (Table 4). There were no other associations with age in North India. In South India there was a positive trend with age for grade 2 AMD ($P = 0.04$). The prevalence of grade 2 was lower in the women than in the men in South India ($P = 0.01$), but there were no differences in the prevalence of other grades of AMD between the sexes in either center (Table 5). Of the 53 persons with late AMD, 44 had CNV (20 in the North and 24 in the South) and 9 had pure GA (3 in the North and 6 in the South).

There were other cases of GA that were categorized with the CNV group. Of the 44 individuals with CNV, 10 also had GA, 7 had GA coexistent with CNV in the same eye, 2 had GA in one eye and coexistent CNV and GA in the other eye, and 1 had GA in one eye and CNV in the other eye.

The modeled age-specific prevalence (95% CI) of late AMD based on the distributions of age, sex, caste, literacy, SES, tobacco use, and BMI in analyses including those with ungradable images was 60 to 64 years, 0.74 (0.70–0.78); 65 to 69 years, 1.11 (1.05–1.16); 70 to 74 years, 1.58 (1.53–1.64); 75 to 79 years, 2.30 (2.21–2.40); 80+ years, 3.54 (3.33–3.77); and all ages studied, 1.34 (1.29–1.39). The estimates for all those enumerated (i.e., including nonattendees and those with ungradable images) were 0.73 (0.71–0.75), 1.10 (1.07–1.12), 1.64 (1.60–1.68), 2.37 (2.32–2.43), and 4.0 (3.85–4.14); and for all ages studied, 1.46 (1.41–1.50).

DISCUSSION

We found a prevalence of late AMD of 1.2% (95% CI, 0.9–1.6) in people aged 60 and older in a population-based study in North and South India. Age-specific prevalence was similar in both centers. The large size of our study ensured narrow 95%

TABLE 3. Age and Sex Standardized Prevalence of Early and Late AMD by Study Center

	North India (*n* = 1995)			South India (*n* = 2271)				Both Centers	
Center	Cases	Prevalence	95% CI	Cases	Prevalence	95% CI	*P*	Prevalence	95% CI
Grade 1*	759	38.0	38.9–40.2	927	40.8	38.8–42.8	0.2	39.5	37.4–41.6
Grade 2†	107	5.4	4.4–6.4	182	8.0	6.9–9.1	0.01	6.7	5.9–7.6
Grade 3‡	1	0.05	0.00–0.1	10	0.4	0.2–0.7	0.05	0.3	0.1–0.4
Grade 4§	23	1.2	0.7–1.6	30	1.3	0.9–1.8	0.6	1.2	0.9–1.6

Data are the % prevalence (95% CI). Age and sex were standardized by using the total study population as the standard.
* Grade 1, presence of soft distinct drusen (≥63 μm) only *or* pigmentary irregularities only.
† Grade 2, soft indistinct (≥125μm) or reticular drusen only *or* soft distinct drusen (≥ 63 μm) with pigmentary irregularities.
‡ Grade 3, (soft indistinct (≥125μm) or reticular drusen) with pigmentary irregularities.
§ Grade 4, choroidal neovascularization (CNV), presence of any of the following: serous or hemorrhagic retinal or retinal pigment epithelial detachment, subretinal neovascular membrane, periretinal fibrous scar *or* geographic atrophy (GA); well-demarcated area of retinal pigment atrophy with visible choroidal vessels.

TABLE 4. Prevalence and 95% CI of Early and Late AMD Grade by Age Group in North and South India

	Age Group (y)					
	60–64	**65–69**	**70–74**	**75–79**	**80+**	***P* Trend by Age**
Grade 1						
North India	37.2	37.2	38.3	40.0	45.8	0.1
	33.5–40.9	32.3–42.0	32.5–44.0	31.2–48.8	32.4–59.3	
South India	39.9	42.0	41.4	39.7	40.6	0.8
	36.8–43.0	37.0–47.0	36.1–46.6	31.8–47.5	32.3–48.9	
Both centers	38.6	39.9	39.9	39.8	43.1	0.2
	36.3–41.0	36.4–43.5	36.0–43.7	34.1–45.5	35.7–50.6	
Grade 2						
North India	4.1	6.2	6.6	7.9	3.1	0.3
	2.1–6.1	4.3–8.2	3.9–9.2	2.7–13.0	0–7.4	
South India	6.7	8.1	9.1	9.2	12.9	0.04
	5.0–8.4	6.0–10.2	6.8–11.5	5.2–13.1	6.6–19.2	
Both centers	5.4	7.3	7.9	8.6	8.1	0.04
	4.1–6.8	5.9–8.7	6.1–9.6	5.4–11.7	4.3–12.0	
Grade 3						
North India	0.1	0	0	0	0	NC
	0–0.4	NC	NC	NC	NC	
South India	0.8	0.3	0	0	1.0	0.3
	0.1–1.4	0–0.7	NC	NC	0–3.1	
Both center	0.5	0.2	0	0	0.5	0.1
	0.1–0.8	0–0.4	NC	NC	0–1.5	
Grade 4						
North India	0.5	1.6	0.8	3.6	2.1	0.01
	0.0–0.9	0.6–2.5	0–1.7	0.6–6.7	0.0–5.1	
South India	0.9	0.9	2.0	2.9	3.0	0.01
	0.3–1.4	0.2–1.5	0.7–3.3	0–5.9	0–6.1	
Both centers	0.7	1.2	1.4	3.2	2.5	0.002
	0.3–1.0	0.6–1.7	0.7–2.2	1.2–5.3	0.4–4.7	

Data are the prevalence (%) and 95% CI. Grades are described in Table 3. NC, not calculated.

CIs around the prevalence rates. The upper range of our CI (1.6) was lower than the estimate of 3% ± 0.4% assumed for our sample size calculations.

A limitation of our results was the proportion of ungradable images, especially in the oldest age groups where AMD prevalence is likely to be the highest. If it is to have a sizeable impact on the overall prevalence estimates, the prevalence of late AMD in people with ungradable images would have to be considerably higher than that found in people with gradable images. For example, we calculated that the age-specific prevalence of late AMD in those with ungradable images would have to be six times higher than in those with gradable ones to achieve an overall prevalence of 2.9%. In the 260 people originally ungradable who had postoperative gradable fundus images, there was only one case (0.4%) of late AMD; 66% had no AMD; and 29% had grade 1, 5% grade 2, and 0.4% ($n = 1$) grade 3. The results suggest a slightly lower prevalence of early and late AMD than that in the group with gradable images. However, the number of people with postoperative images is too small for any conclusions to be drawn. The modeled estimates including those with ungradable images increased the overall prevalence only slightly (from 1.2 to 1.3), but had a larger effect on the prevalence in the oldest age group (80+), from 2.5 to 3.5.

TABLE 5. Prevalence and 95% CI of Early and Late AMD Grade by Sex in North and South India

	Grade 1	**Grade 2**	**Grade 3**	**Grade 4**
Men				
North India	38.9	5.8	0	0.9
($n = 984$)	34.4–43.5	3.9–7.6	NC	0.3–1.6
South India	41.3	9.5	0.4	1.5
($n = 1120$)	38.1–44.5	8.0–11.0	0.0–0.9	0.9–2.2
Both centers	40.2	7.7	0.2	1.2
	37.6–42.8	6.5–9.0	0–0.5	0.8–1.7
Women				
North India	37.2	4.9	0.1	1.4
($n = 1011$)	32.9–41.5	3.4–6.5	0–0.3	0.5–2.3
South India	40.3	6.6	0.4	1.1
($n = 1151$)	36.7–43.9	5.2–8.0	0.0–0.8	0.6–1.7
Both centers	38.9	5.8	0.3	1.2
	36.1–41.6	4.8–6.8	0.1–0.5	0.8–1.7

Data are the prevalence (%) and 95% CI. NC, not calculated.

Response bias may also have led to a lower estimate of AMD in our sample. The oldest age group (80+) was less likely to attend the clinical examination (390/636 enumerated, 61% response) than the youngest age group (60 to 64 years, 2144/2618 enumerated, 82% response) and less likely to have gradable fundus images. Of the enumerated population aged 80 and older, gradable fundus images were available for only 31%. Response bias is suggested by the decline in the age-specific prevalence from 3.2% at 75 to 79 years (95% CI, 1.2–5.3) to 2.5% (95% CI, 0.4–4.7) at 80+ years, whereas, based on studies in Western populations, a substantial increase in the rate in the 80 and older group might be expected. In a study in Western populations in which results were pooled, the prevalence rate in the women rose from 3.4% at 75 to 79 years to 16.4% at 80+ years. Comparable figures for the men were 3.97 and 11.9, respectively.[7] Very similar statistics were reported in the EUREYE study, in which the prevalence of AMD increased from 3.6% at ages 75 to 79 to 12.2% at age 80+.[5] Unfortunately, we have no information to ascertain the number of missed cases of AMD in the 80+ group. At other age groups younger than 80 years, our results are comparable to those for Western studies.[5,7] In the modeled estimates including all nonattendees

TABLE 6. Prevalence of Late AMD in Studies in India

Study	Method of Ascertainment and Grading	Ages 40–49 y	Ages 50–59 y	Ages 60–69 y	Ages 70+ y
ACES[20]	Clinical grading at slit lamp	*N* = 2044	*N* = 1426	*N* = 1099	*N* = 348
N = 4917		*n* = 1	*n* = 6	*n* = 15	*n* = 7
Aged 40+ y	International ARM	GA = 1	GA = 6	GA = 12	GA = 4
		CNV = 0	CNV = 0	CNV = 3	CNV = 3
	Age-specific prevalence, %	0.05	0.42	1.37	2.0
APES[21]	Fundus photo	*N* = 1424	*N* = 1047	*N* = 899	*N* = 353
N = 3723	International ARM	*n* = 13	*n* = 14	*n* = 31	*n* = 13
Aged 40+ y	Age-specific prevalence, %	0.9	1.3	3.4	3.7
INDEYE	Fundus photo	—	*N* = 511	*N* = 352	*N* = 238
Feasibility study[22]	International ARM		*n* = 2	*n* = 2	*n* = 11
			GA = 0	GA = 0	GA = 1
N = 1101			CNV = 2	CNV = 2	CNV = 10
Aged 50+ y	Age-specific prevalence, %	—	0.4	0.6	4.6
	(95% CI)		(0.0–4.0)	(0.1–2.2)	(2.7–7.8)
INDEYE	Fundus photo	—	—	*N* = 2970	*N* = 1296
(Present study)	International ARM			*n* = 26	*n* = 27
n = 4266				GA = 4	GA = 5
Aged 60+ y				CNV = 22	CNV = 22
	Age-specific prevalence, %	—	—	0.88	2.08
	(95% CI)			(0.51–1.24)	(1.31–2.85)

N, number in sample; *n,* number of cases.

and those with ungradable images, AMD prevalence showed a linear increase in age, with the highest prevalence of 4.0% estimated for the 80+ age group. The results from modeling missing data on AMD prevalence suggest that our observed prevalence in the 80+ group was underestimated but it is unlikely that in our study, there is a substantial increase in prevalence in the 80+ group as observed in Western populations.

The prevalence of late AMD was lower in the present study than we found in our feasibility study (Table 6).[22] The feasibility study was conducted only in North India and included people aged 50 years and older with a smaller number of individuals in the older age groups (*n* = 817 aged 60 and older). The differences may be due to sampling error, chance, or unknown biases. Two other population-based studies in India have reported results for late AMD. Both studies recruited participants in the age range 40 years and older. In the Aravind Comprehensive Eye Study (ACES),[20] the prevalence of late AMD (ascertained by clinical grading at the slit lamp) was 1.4% in those 60 to 69 years of age and 2.0% in those 70+ years. In the Andhra Pradesh Eye Study (APES),[21] the prevalence of late AMD (fundus photography) was 3.4% at 60 to 69 years and 3.7% at 70+ years. No information was provided on AMD prevalence in the oldest age groups (i.e., 75–79 and 80+) in ACES and APES, but the number of people 70+ (around 350 in each study) was small. The number in the oldest age groups (80+) was not reported, but was likely to be very small. Information on response rates by age was also not available from the two studies. ACES reported that those without retinal data (mainly due to media opacities) were older than those with data, but no information on ungradable images was reported for the APES, although 39% were reported to have cataract.

In common with studies in Western populations, we found that CNV was the more frequent type of late AMD (83%). This finding was in contrast to the result from the APES and ACES studies, which reported that a higher proportion of AMD was GA (95% in APES and 79% in ACES). Both APES and ACES took place in South India. In our study, proportionately more CNV than GA was reported for both the South India center (24 CNV of 30 late AMD) and the North India center (20 CNV of 23 late AMD). We categorized 10 cases in which GA was present on grading as CNV since, where GA and CNV are coexistent, we consider that the GA is secondary to CNV. In our feasibility study we also found that most late AMD was CNV (14/15 cases). The ACES reported cases of GA but not CNV at young ages (40–49 and 50–59) which is very unusual compared with Western countries, where late AMD is usually not seen below the age of 60. Grading was performed at the slit lamp, a technique that is more prone to error than grading from fundus images, which allow for careful review. Fundus images were used in the APES, but the prevalence by age of GA and CNV was not reported separately. In APES, the prevalence of late AMD was also unusually high at younger ages and was most likely to be due to GA, as most cases in the study (67/71) were GA. It is possible that the higher GA observed in other studies in APES and ACES were due to misclassification of early AMD as GA. It is also possible that we missed some cases of GA, because the darker pigmented retinas of our Indian participants may make it more difficult to see GA.

Comparison of early AMD between studies is more problematic because of variations in methods and reporting. The INDEYE study and the INDEYE feasibility study[22] used identical methods of grading as the EUREYE study facilitating comparison between the studies. Early AMD grade 1 (small soft distinct drusen only or pigmentary irregularities only) was observed in 36.4% (95% CI, 32.7–40.3) of the EUREYE participants 65 years of age and older and in 40.2% (95% CI, 37.5–42.7) in the comparable age range of INDEYE participants. Early AMD grade 2 (large soft indistinct (≥125 μm) or reticular drusen only or soft distinct drusen with pigmentary irregularities) was observed in 10.1% (95% CI, 8.9–11.4) in EUREYE, with similar findings at the South India center (8.9%; 95% CI, 7.6–10.1), and slightly lower results in North India (6.3%; 95% CI, 4.3–8.3). For early AMD grade 3 (soft indistinct or reticular drusen with pigmentary irregularities) the results were different between EUREYE and INDEYE, although in both studies, the prevalence was low, 2.4% in EUREYE (95% CI, 1.8–3.1) and 0.2 (95% CI, 0–0.5) in South India, with only one person with this grading in North India. In our feasibility study in North India, we also found a low prevalence (1.1% in the 60 to 69 age group and 0.8% in the 70+ age group). Moreover, whereas in EUREYE there was a positive increase in AMD3 with age, the trend with

age was inverse in INDEYE and in the feasibility study. In the ACES the prevalence of large drusen with pigmentary irregularities was higher, ranging from 1.3% at 40 to 49 years to 4.9% at 70+ years.

Our results show that the prevalence of late AMD is comparable to that in Western populations, at least in the 60 to 79 age group. The high proportion of ungradable images, along with the lower response rate in the oldest age group (80+), make it likely that the prevalence in this group was underestimated.

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