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# Prevalence of Age-Related Maculopathy in Older Europeans

## *The European Eye Study (EUREYE)*

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**Objective:** To estimate the prevalence of age-related maculopathy in an older population from 7 European countries.

**Methods:** Randomly sampled people 65 years and older were invited to an eye examination in centers across 7 European countries (Norway, Estonia, United Kingdom, France, Italy, Greece, and Spain). Fundus images of each eye were graded at a single reading center. Prevalence rates were calculated for stage of age-related maculopathy with 95% confidence intervals (CIs) estimated for clustered data.

**Results:** Of 5040 participants (45% response rate), 4753 (2128 men and 2625 women) had gradable fundus images. The prevalences were grade 0, 47.59% (95% CI, 43.53%-51.65%); grade 1, 36.48% (95% CI, 32.66%-40.30%); grade 2, 10.14% (95% CI, 8.92% to 11.37%); grade 3, 2.46% (95% CI, 1.79%-3.13%); and grade 4 (age-related macular degeneration [AMD]), 3.32% (95% CI, 2.52%-4.13%) and large drusen only (≥125 μm), 15.41% (95% CI, 13.61%-17.21%). The prevalence of geographic atrophic AMD was 1.2% (95% CI, 0.8%-1.7%) and of neovascular AMD, 2.3% (95% CI, 1.7%-2.9%). The prevalence of bilateral AMD was 1.4% (95% CI, 1.0%-1.8%).

**Conclusion:** Age-specific prevalences of age-related maculopathy in the European Eye Study (EUREYE) are similar to other population-based studies in Western populations.

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AGE-RELATED MACULAR DEgeneration (AMD) is the most important cause of adult blindness in developed countries and the third cause of global blindness.[1,2] There are 2 main types of AMD: neovascular AMD (NV-AMD), characterized by invasion of the subpigment epithelial and subretinal spaces by neovascular complexes known as choroidal neovascularization, and geographic atrophy (GA), characterized by extensive loss of the choriocapillaris and the overlying retinal pigment epithelium. The ratio of visually impairing NV-AMD to GA is around 2-fold.[3] Age-related macular degeneration is considered to represent the late stage of a constellation of morphological changes in the retina that occur in the aging eye and are collectively called age-related maculopathy (ARM). Early changes, especially yellowish deposits (drusen), along with abnormalities of pigmentation and patchy atrophy of the retinal pigment epithelium are found in the older population but are not usually associated with vision loss. Longitudinal studies have shown that these features are a risk factor for the development of AMD, although the proportion who develop AMD is relatively small and dependent on the type of AMD studied, morphological changes, age, and length of follow-up.[4-7] The prevalence of ARM and AMD has been described in different population settings, predominantly in developed countries[8] such as the United States,[9] Australia,[10,11] and Europe.[12-17] All but one of the European studies were undertaken in northern Europe,[13-16] including Iceland.[17] Of the European studies, 3 were very small (<500 participants)[12,14,15] or because of the younger age range studied had only a small number of cases of AMD[13,17]; only 2 used grading methods that permitted comparisons with other studies.[13,17] The European Eye Study (EUREYE) was developed to provide estimates of the prevalence of ARM and AMD in a wider European context using a common protocol for ophthalmic examination and grading and to examine asso-

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ciations with lifestyle and environmental factors, with a particular focus on solar radiation and dietary antioxidants. In this article, we report the results for prevalence.

## METHODS

### STUDY DESIGN

The EUREYE Study is multicenter, population-based cross-sectional study with retrospective and current exposure measurements. A detailed description of the study design has been reported.[18] Briefly, 7 study centers, Bergen, Norway; Tallinn, Estonia; Belfast, Northern Ireland, United Kingdom; Paris-Creteil, France; Verona, Italy; Thessaloniki, Greece; and Alicante, Spain, were chosen primarily to maximize the range of latitude and lifestyle behaviors, including diet. The EUREYE Study aimed to enroll 800 to 900 persons 65 years and older in each of the 7 centers. The sample size calculations estimated that 6000 people would be required to detect a prevalence of AMD of mean ± SD 2% ± 0.5% at 95% confidence and a design effect of 2, to allow for the cluster (ie, country) effects. The sampling frame consisted of all persons 65 years or older who were included in the National Population Registry (Estonia), Patient Register (Northern Ireland, which includes all people registered with family physicians—around 98% of the local population), National Office for Statistics (Spain), and Municipal Register (France, Greece, Italy, and Norway) at the time the sample was requested. In each center, the random sample was drawn by the statistical officers at the registries. Ethics approval was obtained at each center from the relevant ethics committee. Study participants gave informed written consent prior to participation.

### MEASUREMENTS

Study participants were interviewed by trained fieldworkers using structured questionnaires for smoking and alcohol use, brief medical history, dietary habits (food frequency questionnaire), outdoor occupational and leisure behavior, and vision-related quality of life. These questionnaires were administered prior to the ophthalmological examination. Distance visual acuity was recorded in each eye separately using the Early Treatment of Diabetic Retinopathy Study logarithm of the minimum angle of resolution (logMAR) chart. The testing distance was 4 m, and if a participant was unable to read 20 letters at this distance, the test was repeated at 1 m. Any participant who was unable to achieve a 0.3 logMAR (Snellen 20/40) in either eye underwent automatic or manual retinoscopy followed by refraction and recording of best-corrected acuity. Slitlamp biomicroscopy was used to examine the anterior and posterior ocular segments. Pupillary dilation was achieved using 0.5% tropicamide and/or 2.5% phenylephrine hydrochloride. Stereo fundus photography was then performed.

### FUNDUS PHOTOGRAPHY AND IMAGE GRADING

In a preliminary validation study, we investigated whether grading of digitally captured images would be comparable with grading on color transparencies (which has been the standard procedure in epidemiologic studies to date).[19] Two experienced graders graded both analog and digital images of identical eyes, and the weighted $\kappa$ value for between-technique agreement was 0.76 overall. For AMD, agreement was excellent with a weighted $\kappa$ of 0.94 for NV-AMD and 0.87 for GA. These findings supported the use of digital photography in EUREYE. All centers were equipped with a digital Topcon fundus camera (TRC-50EX; Topcon Corporation, Tokyo, Japan). Capture settings were calibrated and standardized for all 7 centers. For each eye, two 35° nonsimultaneous stereoscopic color fundus images were taken, centered on the fovea. Images were saved without manipulation as raw TIFF files to CDs and sent to the grading center in Rotterdam (P.T.V.M.J. and J.R.V.). Grading was undertaken by the same graders using a protocol identical to that of the validation study. Briefly, images were examined on a Sony E500 21-inch FD Trinitron CRT monitor (0.24-mm aperture grille pitch) (Sony Electronics Inc, Park Ridge, NJ). The monitor was set at 32 bits true color and 1280 × 1024 pixel resolution at 103 Hz. Stereo pairs were displayed side by side on the monitor using the "compare images" module of ImageNet (Topcon) and examined with a handheld stereo viewer at a distance of 50 cm. The monitor provided a 10-fold increase in image size, resulting in a total magnification of approximately × 25. No image manipulation was used before or during grading.

The definitions of ARM were based on the International Classification System for ARM.[20] In this system, features within a fixed area (diameter, 6000 μm) around the fovea are recorded. This area was delineated by a grid consisting of 3 concentric circles and a right-angled cross at 45° and 135° to the horizontal. The diameters of the central, inner, and outer circle were 1000 μm, 3000 μm, and 6000 μm, respectively. Drusen were categorized on the basis of their appearance, namely, size; homogeneity of surface features; and outlines. Pigmentary irregularities were classified into either hypopigmentation or hyperpigmentation. When GA and NV-AMD coexisted in the same eye, this was categorized as NV-AMD. When in doubt, eyes with other disorders resembling AMD were not categorized as AMD. The signs of ARM were stratified using the Rotterdam staging system into 5 exclusive stages (ARM, 0-4) to facilitate analysis.[4] Three ophthalmologists (J.R.V., P.T.V.M.J., and U.C.) scrutinized all fundus images assigned to AMD (GA or NV-AMD) and adjudicated on any questionable lesions. No information other than age and center was available to the graders or ophthalmologists during grading or adjudication.

### DATA COLLECTION AND ANALYSIS

Study coordination was undertaken at the London School of Hygiene and Tropical Medicine (A.E.F. and C.A.A.). Data from the 7 centers were sent to the London School of Hygiene and Tropical Medicine for data processing, cleaning, and merging with the grading results sent separately from the grading center. Standard procedures for data checks and editing were carried out. Statistical analysis was carried out using Stata 8.[21] Prevalences were based on the highest grade in the worst eye. Age and sex standardization using the study population as the standard (direct standardization) were carried out for prevalence by center. Sex standardization was used to compare prevalence by age group (65-69, 70-74, 75-79, and ≥80 years) and age standardization, for prevalence by sex. We also examined the prevalence of large drusen (≥125 μm) for comparison with results from an international meta-analysis.[22] Poisson regression was undertaken to estimate effects of age adjusted for sex and for sex adjusted for age on the prevalence of ARM and on large drusen.[23] Age was included as a continuous and squared term. All analyses took account of the survey design (7 centers) in the estimation of standard errors and corresponding *P* values and 95% confidence intervals (CIs).

## RESULTS

The majority of study participants were recruited during a 1-year period in all centers. In calculating participation rates, we counted all persons who underwent at

**Table 1. Participation Rates by Age, Sex, and Study Center**

| | Men | | | | | Women | | | | | All Men and Women |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | 65-74 y | | ≥75 y | | All | 65-74 y | | ≥75 y | | All | |
| Study Center | No. Invited | Response Rate, % | No. Invited | Response Rate, % | Response Rate, % | No. Invited | Response Rate, % | No. Invited | Response Rate, % | Response Rate, % | Response Rate, % |
| Bergen, Norway | 362 | 66.0 | 187 | 55.1 | 62.3 | 469 | 57.8 | 336 | 43.8 | 51.9 | 56.1 |
| Tallinn, Estonia | 398 | 61.1 | 159 | 57.2 | 60.0 | 638 | 59.2 | 483 | 56.3 | 58.0 | 58.6 |
| Belfast, Northern Ireland | 371 | 58.2 | 352 | 34.9 | 46.9 | 402 | 47.5 | 609 | 24.8 | 33.8 | 39.3 |
| Paris-Creteil, France | 372 | 52.7 | 227 | 49.3 | 51.4 | 518 | 57.7 | 457 | 35.2 | 47.2 | 48.4 |
| Verona, Italy | 387 | 50.6 | 271 | 37.3 | 45.1 | 618 | 35.0 | 474 | 21.5 | 29.1 | 35.1 |
| Thessaloniki, Greece | 629 | 42.9 | 205 | 36.7 | 41.1 | 684 | 32.7 | 229 | 27.8 | 31.5 | 36.1 |
| Alicante, Spain | 351 | 52.4 | 167 | 52.7 | 52.5 | 460 | 44.3 | 319 | 39.2 | 42.2 | 48.3 |
| Total | **2870** | 51.8 | **1568** | 45.3 | 50.4 | **3789** | 45.7 | **2907** | 35.5 | 41.9 | 45.3 |

**Table 2. Prevalence of Age-Related Maculopathy (ARM) Grade and Presence of Large Drusen by Study Center***

| | | ARM Grade | | | | | |
|---|---|---|---|---|---|---|---|
| Study Center | Sample Size | 0 (n = 2262) | 1 (n = 1734) | 2 (n = 482) | 3 (n = 117) | 4 (n = 158) | Large Drusen (n = 730)† |
| Bergen, Norway | 744 | 51.31 (47.76-54.85) | 32.34 (28.99-35.70) | 9.81 (7.70-11.93) | 3.07 (1.85-4.30) | 3.46 (2.23-4.69) | 16.03 (13.45-18.61) |
| Tallinn, Estonia | 914 | 43.63 (40.4-46.94) | 37.79 (34.56-41.02) | 11.61 (9.44-13.77) | 3.18 (2.00-4.35) | 3.79 (2.58-5.00) | 15.15 (12.83-17.46) |
| Belfast, Northern Ireland | 634 | 51.53 (47.59-55.46) | 31.79 (28.09-35.50) | 10.65 (8.29-13.00) | 2.26 (1.18-3.34) | 3.77 (2.28-5.27) | 13.10 (10.49-15.71) |
| Paris-Creteil, France | 703 | 41.54 (37.90-45.18) | 43.95 (40.26-47.64) | 9.22 (7.10-11.36) | 2.27 (1.21-3.34) | 3.02 (1.79-4.25) | 18.40 (15.58-21.21) |
| Verona, Italy | 605 | 46.19 (42.21-50.16) | 36.77 (32.97-40.56) | 11.19 (8.68-13.71) | 2.18 (1.00-3.35) | 3.68 (2.17-5.18) | 13.73 (10.98-16.49) |
| Thessaloniki, Greece | 587 | 49.45 (44.94-53.95) | 35.63 (31.22-40.03) | 8.30 (6.12-10.48) | 1.92 (0.02-3.64) | 4.71 (2.44-6.97) | 14.82 (11.39-18.24) |
| Alicante, Spain | 566 | 51.77 (47.71-55.82) | 37.24 (33.37-41.13) | 7.84 (5.63-10.04) | 1.81 (0.08-2.86) | 1.34 (0.42-2.23) | 14.57 (11.68-17.47) |
| *P* value for homogeneity | | .02 | .004 | .30 | .70 | .20 | .10 |
| Total | **4753** | 47.59 (43.53-51.65) | 36.48 (32.66-40.30) | 10.14 (8.92-11.37) | 2.46 (1.79-3.13) | 3.32 (2.52-4.13) | 15.41 (13.61-17.21) |

*Values are expressed as percentage (95% confidence interval) unless otherwise indicated. Prevalence rates by center were age and sex standardized using the total study population as the standard. ARM grade 0: absence of any of the features of grades 1 to 4; ARM grade 1: presence of soft, distinct drusen (≥63 µm and <125µm) only or pigmentary irregularities only; ARM grade 2: soft, indistinct (≥125 µm) or reticular drusen only or soft, distinct drusen with pigmentary irregularities; ARM grade 3: soft, indistinct, or reticular drusen with pigmentary irregularities; ARM grade 4: neovascular age-related macular degeneration (presence of any of the following: serous or hemorrhagic retinal or retinal pigment epithelial detachment, subretinal neovascular membrane, or periretinal fibrous scar or geographic atrophy; well-demarcated area of retinal pigment atrophy with visible choroidal vessels).

†Information missing for 16 people.

least 1 interview or ophthalmological examination. The overall participation rate was 45.3% and lower in the older age groups (38.3% aged ≥75 years compared with 50.0% aged 65-74 years) and in women compared with men (41.9% and 50.4%) (**Table 1**). Of the 5040 who agreed to take part, 4935 both attended the clinical examination and responded to the interview questions; of these, 4831 underwent fundus photography, of which at least 1 fundus image could be graded for 4753 participants. One hundred five did not attend the clinical examination but completed the interview. The great majority of participants were white Europeans who were born in the country of the participating center. The only exception to this was Paris-Creteil where 17% of the participants were born in North Africa, but because we did not have data on ethnic origin, we were unable to ascertain if they were of European or Arabic descent.

Approximately half of all people, 47.59% (95% CI, 43.53%-51.65%) had no or minimal morphological changes (no drusen or small drusen <63 µm in diameter) in either eye (grade 0) (**Table 2**). Just more than a third of all participants, 36.48% (95% CI, 32.66%-40.30%), had signs of ARM grade 1. There was a slightly lower prevalence of ARM grade 0 and a higher prevalence of ARM grade 1 for Paris-Creteil compared with other centers. The differences in prevalence were of small magnitude (<10%). The prevalence of ARM grade 2 was 10.14% (95% CI, 8.92%-11.37%); of ARM grade 3, 2.46% (95% CI, 1.79%-3.13%); and of ARM grade 4 (AMD), 3.32% (95% CI, 2.52%-4.13%). The overall prevalence of large drusen (≥125 µm) was 15.41% (95% CI, 13.61%-17.21%). There were strong inverse trends with age for ARM grade 0 ($P<.001$) and ARM grade 1 ($P<.01$) and positive trends for ARM grades 2 to 4 and large drusen (**Figure 1**). The prevalence of ARM grade 2 was lower in women than men (age-adjusted prevalence ratio, 0.8 [95% CI, 0.6-0.9]), whereas AMD was more prevalent in women than men but the 95% CIs crossed unity (age-adjusted prevalence ratio, 1.4 [95% CI, 0.9%-1.8%]) (**Figure 2**).

Of the 158 cases of AMD, 49 had only GA (26 bilateral and 23 unilateral), 8 people had GA in one eye and NV-AMD in the other eye, and 101 had NV-AMD only

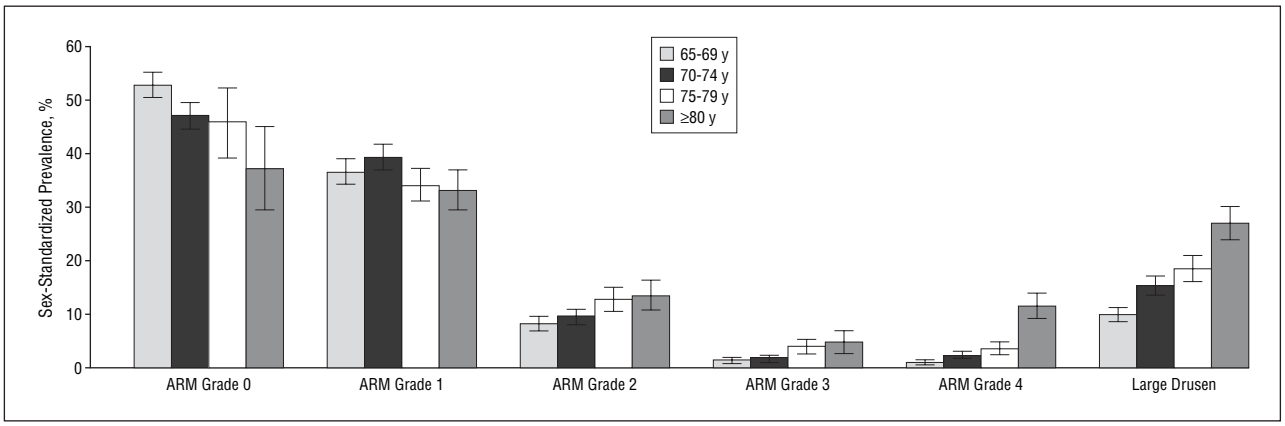


**Figure 1.** Prevalence of age-related maculopathy (ARM) grades and presence of large drusen in the study population by age group. Error bars represent 95% confidence intervals.

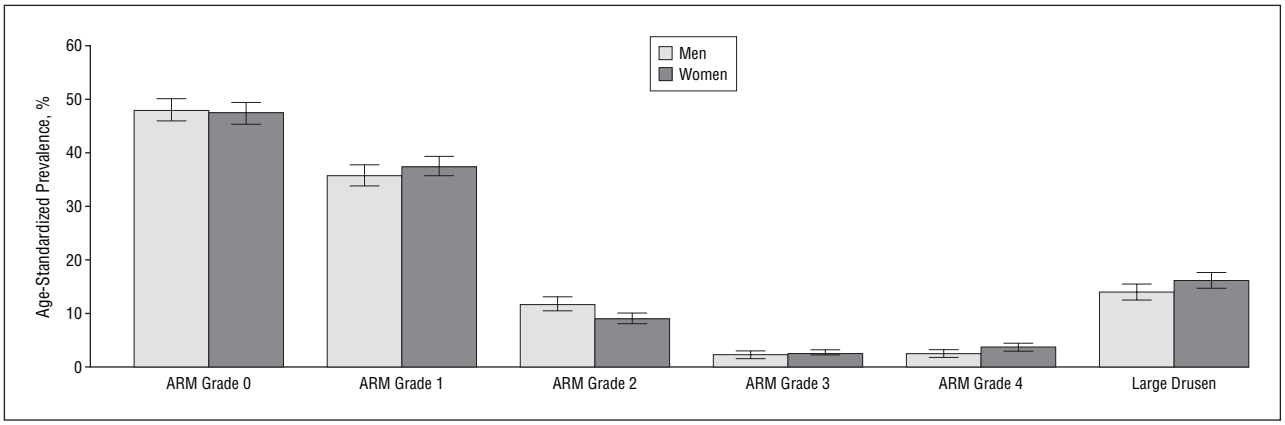


**Figure 2.** Age-adjusted prevalence ratios for age-related maculopathy (ARM) grades and presence of large drusen in the study population by sex. Error bars represent 95% confidence intervals.

(40 bilateral and 61 unilateral). In 33 cases, GA and NV-AMD occurred in the same eye and these were included in the estimates for NV-AMD but not for GA. The prevalence of GA (including cases with NV-AMD in the other eye) was 1.2% (95% CI, 0.8%-1.7%) and for NV-AMD (including cases with GA in the other eye), 2.3% (95% CI, 1.7%-2.9%) (**Table 3**). Bilateral AMD (either GA or NV-AMD) occurred in 66 people overall, 1.4% (95% CI, 1.0%-1.8%), but there were no differences by age or sex compared with people with unilateral AMD.

## COMMENT

To our knowledge, EUREYE is the first study to obtain prevalence estimates of ARM and AMD across a variety of European populations using a common protocol and single grading center. A few single-center studies of ARM in the European setting have been undertaken but most have been small[12,15] or used noncomparable grading systems.[14,16]

The EUREYE Study used digital fundus photography with independent grading by a single reading center with identical methods for grading as the Rotterdam Study.[19] The same type of camera was used in all centers. Digital photography permits images to be checked for quality at the time of acquisition and repeated if necessary, thus obviating the need to recall the participant. Of images taken in EUREYE, 98% were gradable. The criteria for grading the images were established prior to data collection and graders were unaware of any findings on the clinical examinations or risk factor exposures of the study participants, other than age.

The participation rate in EUREYE was 45% and varied by age and sex, being lower in women and in the older age group. Participation rates overall in other studies have varied between 54% and 95%[24] but not all studies have reported participation rates by age group or sex. In several studies, the inclusion criteria were younger by 1 to 2 decades[9-11,13,17] compared with our study, with commensurately higher response rates in the younger age groups. Most studies use a number of tactics to increase participation. For example, eligible participants may be repeatedly invited (10 attempts in the Melbourne Visual Impairment Project[11]), financial incentives may be offered, or field workers sent to make direct contact to encourage participation. In EUREYE, centers were restricted by their ethics committees to defined modes of contact. Invitation was by a maximum of 3 letters sent during a period of 8 to 10 months. People who refused could not be recontacted because ethics committees regarded this as unacceptable, and in some centers, reasons for refusal or any other information from refusers

**Table 3. Prevalence of Geographic Atrophy (GA) and Neovascular Age-Related Macular Degeneration (NV-AMD) and Presence of Large Drusen by Sex and Age Group***

| | Sample Size | Any AMD | | NV-AMD in Either Eye | | GA in Either Eye | | Drusen ≥125 µm | |
|---|---|---|---|---|---|---|---|---|---|
| | | EUREYE | Pooled Data | EUREYE | Pooled Data | EUREYE | Pooled Data | EUREYE | Pooled Data |
| Men | | | | | | | | | |
| 65-69 y | 782 | 0.90 (0-2.08) | 1.08 (0.91-1.29) | 0.38 (0-1.01) | 0.73 (0.61-0.87) | 0.51 (0-1.10) | 0.66 (0.56-0.76) | 9.73 (7.53-11.93) | 7.48 (6.74-8.28) |
| 70-74 y | 712 | 1.97 (0.77-3.17) | 1.98 (1.69-2.32) | 1.40 (0.51-2.29) | 1.33 (1.14-1.56) | 0.56 (0-1.06) | 1.19 (1.04-1.37) | 12.52 (9.86-15.17) | 10.40 (9.29-11.63) |
| 75-79 y | 418 | 4.07 (1.86-6.27) | 3.97 (3.18-4.24) | 2.63 (0.78-4.49) | 2.49 (2.15-2.88) | 1.91 (0-4.10) | 2.16 (1.91-2.46) | 18.66 (12.31-25.01) | 14.30 (12.55-16.25) |
| ≥80 y | 216 | 6.94 (1.06-12.83) | 11.90 (9.78-14.41) | 5.56 (0-11.48) | 8.29 (6.76-11.20) | 1.39 (0.01-2.77) | 6.60 (5.52-7.89) | 23.26 (15.75-30.76) | 25.62 (21.69-29.98) |
| All | 2128 | 2.49 (2.07-2.91) | NA | 1.69 (1.11-2.27) | NA | 0.89 (0.49-1.30) | NA | 13.78 (11.36-16.21) | NA |
| Women | | | | | | | | | |
| 65-69 y | 871 | 1.03 (0.11-1.96) | 0.70 (0.64-0.76) | 0.92 (0.04-1.80) | 0.51 (0.45-0.59) | 0.11 (0-0.40) | 0.37 (0.34-0.40) | 9.89 (8.28-11.49) | 7.81 (7.30-8.34) |
| 70-74 y | 846 | 2.36 (1.00-3.73) | 1.52 (1.41-1.64) | 1.42 (0.34-2.50) | 1.09 (0.96-1.24) | 0.95 (0.34-1.55) | 0.81 (0.74-0.88) | 17.29 (13.82-20.78) | 11.17 (10.39-12.00) |
| 75-79 y | 508 | 3.15 (2.02-4.28) | 3.44 (3.22-3.69) | 2.17 (0.96-3.37) | 2.40 (2.14-2.70) | 1.18 (0-2.39) | 1.85 (1.72-1.99) | 18.09 (14.52-21.66) | 15.73 (14.48-17.06) |
| ≥80 y | 400 | 15.00 (9.63-20.37) | 16.39 (14.97-17.91) | 10.50 (6.65-14.35) | 11.07 (9.46-12.91) | 5.75 (2.67-8.83) | 9.37 (8.53-12.9) | 28.86 (20.88-36.84) | 29.16 (26.34-32.15) |
| All | 2625 | 4.00 (2.86-5.14) | NA | 2.78 (2.09-3.47) | NA | 1.45 (0.74-2.16) | NA | 16.73 (14.63-18.82) | NA |
| Total | 4753 | 3.32 (2.52-4.13) | NA | 2.29 (1.73-2.86) | NA | 1.20 (0.75-1.65) | NA | 15.41 (13.61-17.21) | NA |

Abbreviations: EUREYE, European Eye Study; NA, not available.
*Values are expressed as percentage (95% confidence interval) unless otherwise indicated.

could not be collected as a consequence of similar concerns by ethics committees. As a result of the lower response rate, we recruited fewer participants than estimated for our sample size calculations. The prevalence of AMD was higher than originally assumed (3.3% observed compared with 2% expected), and the design effect (ratio of variance observed under cluster sampling to variance under simple random sampling) was lower (1.6 observed compared with 2 expected). The precision of our estimate was within ±0.8%, slightly higher than the 0.5% for our sample size calculations.

The effect of the low response rate on our estimates is uncertain; in particular, whether response bias is related to AMD. People with AMD under the care of hospital clinics might be less likely to participate and bias the estimates downward; conversely, people with undiagnosed problems may be more willing to attend than those without and bias the estimates upward. A healthy participant effect would result in a reduced estimate of prevalence. Unfortunately, we were not able to collect any information on the vision status of nonrespondents. Our prevalence figures for AMD, type of AMD, and large drusen were comparable with those reported for white men and women of a similar age in a pooled analysis of the major population-based studies using fundus photography and comparable grading systems[22] (Table 3). For both men and women, the prevalence of large drusen was consistently a little higher in EUREYE for all age groups except the oldest age groups where the prevalence was very similar to the EUREYE prevalence estimates, falling within the 95% CIs of the estimates from the pooled analysis of the population studies. In men, the prevalence of AMD was similar except for the oldest age group (≥80 years) where the prevalence in EUREYE (6.9% [95% CI, 1.1%-12.4%]) was lower than in the pooled estimates (11.9% [95% CI, 9.8%-14.4%]); for women, the prevalence rates for AMD from EUREYE were very similar to those in the pooling study. All 95% CIs for EUREYE for AMD included the point estimates from the pooling study reflecting the wider CIs from EUREYE. Moreover, the estimates for the oldest age group (≥80 years) will vary according to the proportions of people at different ages in that group. For more rigorous comparisons, age-standardized estimates are required. For GA, our estimates tended to be lower than in the pooling studies, although, in common with the pooling project, we excluded people with GA and NV-AMD in the same eye on the basis that in these cases GA was secondary to NV-AMD. We should be cautious not to overinterpret differences between EUREYE and the pooling study since the studies contributing to the pooled results themselves showed quite wide variation in prevalence estimates, for example a 2-fold range in the prevalence of AMD in the groups 75 years and older between the highest and lowest estimates of the individual 7 studies contributing to the pooled results. The Rotterdam Study, the only European study in the pooling study, had a slightly lower prevalence of AMD compared with some other studies but this was (as reported in an earlier study) owing to a lower prevalence of neovascular AMD in Rotterdam

whereas the prevalence of GA was similar to that observed in other studies.[25] Our estimates for GA for the group 65 years and older are close to those reported for the comparable age group in the Blue Mountains Eye Study and the Beaver Dam Eye Study.[25] Estimates for GA and NV-AMD from the individual studies of the pooling study are not presented, but it is possible that the estimates also show a wide variation between the 7 studies.

There was a suggestion of a higher prevalence of AMD in women compared with men, especially for bilateral AMD. A higher prevalence of AMD in women was reported in the Beaver Dam Eye Study (odds ratio [OR], 1.16) and the Blue Mountains Eye Study (OR, 1.35) and a lower prevalence in the Rotterdam Study (OR, 0.82), although none of these results was significant.[25] In a UK study of visually impairing AMD in people 75 years and older, women had a higher rate at all ages (OR, 1.4 [95% CI, 1.0-1.9]).[26] In the pooled analysis of the major population-based studies, the overall rates of AMD were similar in white men and women except for the age group older than 80 years (16.4% in women compared with 11.9% in men)[22] (Table 3). It is possible that the higher rates observed for women at older ages may reflect differential survival if men with ARM or AMD are more likely to die at earlier ages. Although studies have not found an independent association of AMD or ARM with mortality after adjustment for confounders,[27-31] it is plausible that selective survival may have occurred (ie, the higher prevalence of smoking and diabetes mellitus in men in middle age and the strong associations of these factors with mortality may have removed the most susceptible from the population). In EUREYE, adjustment for smoking and diabetes (additionally to age) considerably increased the association observed for women with AMD (prevalence ratio, 1.8 [95% CI, 1.3-2.5]). It is also possible that different characteristics of nonresponders in women compared with men may have biased the results (eg, if response in women was more likely to be associated with AMD), but we have no data to investigate this. We found an excess of NV-AMD (prevalence of 2.3%) compared with GA (prevalence of 1.2%), a ratio of 1.9, similar to ratios reported in other studies.[9,10,13] A recent article suggested that the prevalence of GA in Iceland was considerably higher than observed in other European populations or populations of European ancestry,[17] with an overall prevalence in their older than 50 years population of 3.2% for GA (29 cases) and 0.7% (6 cases) for NV-AMD, a ratio of 0.22. In that study, of men and women 80 years and older, 25% had GA compared with 9.8% with NV-AMD. The authors speculated that genetic or dietary factors might account for the higher rates of GA. In EUREYE, there was only 1 Scandinavian center (Norway), but although the number of cases was small, there was no evidence that GA was more common; the ratio was 1.8 based on 18 cases of NV-AMD (2.4%) and 10 cases (1.3%) of GA, including 1 case with both GA and NV-AMD.

Based on the findings from EUREYE, we estimate that 3.3% (95% CI, 2.5%-4.1%) of the European population 65 years and older have AMD in at least one eye. However, the lower participation rate in our study means that these estimates may be subject to selection bias. If the figure of 3.3% found in this study is applied to the population 65 years and older of the European Union, an estimated 2.5 million have AMD and more than 1.1 million have the visually disabling disorder of bilateral AMD.

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