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Prevalence of age-related macular degeneration in the Republic of Ireland

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ABSTRACT

Background Age-related macular degeneration (AMD) remains the most common cause of visual loss among subjects over 50 years of age in the developed world. The Irish Longitudinal study on Ageing (TILDA) is a population-based study of subjects aged 50 years or older, designed to investigate factors that influence ageing, and has enabled this investigation of the prevalence of AMD in the Republic of Ireland (ROI).

Methods Data collected from a nationally representative sample of community-living older adults aged 50 years and over in ROI over the period November 2009 to July 2011. 5035 participants attended the TILDA health centre for assessment. Retinal photographs were obtained in 4859 of these participants. Retinal grading was performed in a masked fashion using a modified version of the International Classification and Grading System for AMD.

Results Adjusting for lower response rates among older subjects, the estimated overall prevalence of any AMD was 7.2% (95% CI 6.5% to 7.9%) in the population aged 50 years or older. The estimated prevalence of early AMD was 6.6% (95% CI 5.9% to 7.3%), and the estimated prevalence of late AMD was 0.6% (95% CI 0.4% to 0.8%). Statistically significant associations with AMD included increasing age and family history of the condition.

Conclusions This is the first study to provide prevalence estimates of AMD in ROI and will inform eye care professionals and policymakers involved in the delivery and planning of care for those afflicted with this condition.

INTRODUCTION

Age-related macular degeneration (AMD) is the leading cause of blind registration in the developed world. In the Republic of Ireland (ROI), AMD is estimated to account for 25% of all blind registration (57.1 per 100 000 adults).[1] Early AMD is characterised by drusen and/or pigmentary abnormalities, whereas the late (advanced) form of AMD is visually consequential and can be classed as atrophic (geographic atrophy) or neovascular.[2]

Subjects with early AMD benefit from antioxidant supplementation, in terms of reduced risk of visual loss and disease progression.[3 4] Currently, there is no effective treatment for atrophic AMD, whereas neovascular AMD is treated by intravitreal injections of antivascular endothelial growth factor therapy.[5 6] The ongoing nature of treatment for neovascular AMD has profound cost implications to patients and to society, reflected in the recent retrospective observational study that demonstrated that new cases of neovascular AMD were associated with substantial discrepancies in total medical costs (41% higher compared with non-neovascular AMD controls).[7] The cost implications for neovascular AMD treatment are, however, balanced against savings associated with this treatment (improvement in visual acuity and reduction in cases of legal blindness).[8] Patients with untreated or untreatable advanced AMD invariably suffer from impairment of central vision, with consequential loss of social independence as a result of a concomitant inability to read, recognise faces, watch television or drive.[9]

The Irish Longitudinal Study on Ageing (TILDA, http://www.tilda.ie)[10] is a prospective cohort study aimed at providing representative and comprehensive data relating to older people and the ageing population in ROI, by collecting data on the social, economic and health status of participants aged 50 years and over. At baseline (wave 1), TILDA collected vision data, including retinal photographs for grading of AMD, as part of the health assessment.

Although the prevalence of AMD has been reported in population-based studies for many different countries,[11 12] the TILDA sample provides an unprecedented opportunity to investigate the prevalence of AMD from a population-based random sample selected from ROI.

MATERIALS AND METHODS

Study population

The design and methodology of TILDA has been described in detail elsewhere.[10] The TILDA sampling frame was based on a comprehensive record of all residential addresses in ROI compiled by the Irish Postal Service (An Post) and Ordnance Survey Ireland (RANSAM system, developed by the Economic and Social Research Institute of Ireland), and the sampling method was designed to achieve a population-representative sample of (community-resident) individuals aged 50 years or older. The sampling frame was made up of 3155 clusters (500–1180 residential addresses in each cluster). A total of 640 clusters were randomly selected using proportionate stratification by socioeconomic status (percentage in professional/managerial occupations), age structure (percentage of population aged 50 years or older) and geography. Forty residential addresses were randomly selected from each of the 640 clusters, resulting in a list of 25 600 addresses. A letter of invitation was sent to each of the sampled addresses, furnishing residents with information about the study and informing residents of the

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proposed visit by a member of the field staff. All sampled addresses were then visited by a member of the field staff, and residents that were deemed eligible were then invited to participate. All persons aged 50 years and over (primary respondents) and their spouses or partners of any age (secondary respondents) were eligible for inclusion in TILDA. Of note, secondary respondents are not included in this analysis.

In all, 8504 participants were sampled, with 8175 participants aged 50 years or older. Enrolled participants completed the computer-assisted personal interviewing questionnaire, self-completion questionnaires and were offered either a health centre assessment or a home-based assessment.[10 13] Of note, 5035 (62%) participants underwent a health centre assessment, which included retinal photographs for AMD grading. Figure 1 illustrates the TILDA baseline (wave 1) participants included in the current study. Data for this report were collected as part of the first wave of TILDA, which was initiated in October 2009, and completed in July 2011.

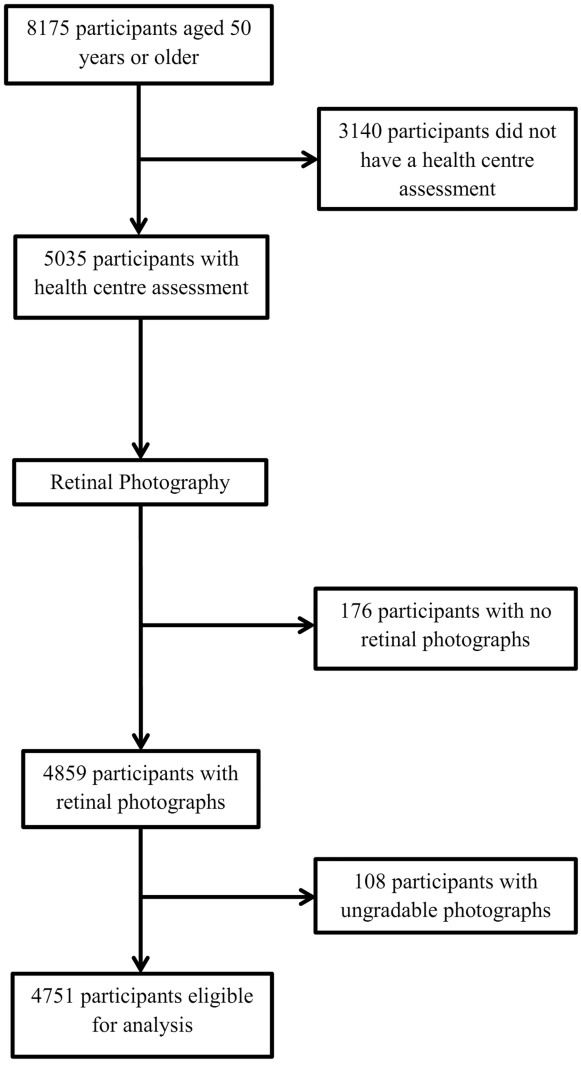

Figure 1 A total of 8175 participants aged 50 years or older completed the Irish Longitudinal study on Ageing (TILDA) baseline (wave 1) interview. Health assessments were conducted in clinical centres in Dublin and Cork, Republic of Ireland. Participants who refused or were unable to attend clinical centres were given the option of a home-based clinical assessment. Home-based clinical assessment did not include retinal photography. Retinal photographs were taken at the clinical centres using the NIDEK AFC-210 camera. Subjects with no photographs were either due to the following reasons: unable, unwilling and technical failure. Photographs were judged as ungradable based on photographic quality.

Retinal photography

Retinal photography was carried out using the NIDEK AFC-210 non-mydriatic auto-fundus camera, through a non-dilated pupil, by TILDA research nurses. TILDA nurses were trained and certified by experts from the Ocular Epidemiology Reading Centre at the University of Wisconsin, Madison, USA. One 45° monoscopic colour photograph, centred on the macula (Early Treatment Diabetic Retinopathy Study standard field 2), was obtained for each eye. The photographs were anonymised using a unique identifier and transferred to the Moorfields Eye Hospital (MEH) Reading Centre, London, UK (http://www.readingcentre.org) and the Macular Pigment Research Group (MPRG, http://www.mprg.ie), Vision Research Centre, Waterford, Ireland.

Retinal grading

Retinal photographs were graded at MPRG, Vision Research Centre, Waterford, Ireland, by a masked grader (KOA) who was trained and certified at the MEH Reading Centre. Grading was carried out under the supervision of the MEH Reading centre manager (TP) using a modified version of the International Classification and Grading System for AMD.[2]

The following AMD features were evaluated: the presence of >10 hard drusen (<63 μm), soft drusen (>125 μm), atrophic AMD and signs of neovascular AMD (choroidal neovascularisation, retinal pigment epithelium detachment, disciform scar). Early AMD was defined as the presence of >10 hard drusen (<63 μm) and/or the presence of soft drusen (>125 μm). Late AMD was defined as the presence of atrophic AMD and/or neovascular AMD. Mixed AMD was defined as the presence of atrophic AMD in one eye and neovascular AMD in the other eye.

AMD features graded as questionable were adjudicated by the MEH Reading Centre. To ensure that valid and reliable data with respect to AMD grading were secured, the following quality assurance measures were taken: first, 10% of images were regraded by the MEH Reading Centre for concordance. Second, intragrader reliability was assessed by the regrading of a 3% randomly selected sample of retinal photographs graded by the principal grader (KOA) with a minimum interval of 14 days between visualisation of the images in question.

Statistical analysis

Statistical analysis was conducted using IBM SPSS Statistics for Windows, V.20.0. Armonk, New York, New York, USA; weighted kappa statistics, not available in SPSS, were obtained using the statistical programming language R.[14] For purposes of statistical analysis, the worst eye, in terms of AMD severity, was assigned to each participant.

Of 5035 TILDA participants who presented at health centres for clinical examination, 4859 had retinal photographs for at least one eye (right eye in 4808 and left eye in 4798). Intragrader reliability was assessed in 300 eyes using the kappa statistic. Demographic characteristics of participants with gradable photographs were compared with those with ungradable photographs using independent samples t test or χ^2 test of independence. After excluding subjects with ungradable fundus photographs, 4751 participants remained for estimating AMD prevalence.

Selection of households for inclusion in this study was random, but we identified two major sources of subsequent bias. In addition to the usual non-response bias, common to most social surveys, it was evident that non-attendance at health

centres was more common, for example, among older subjects, and this introduced additional bias. In order to identify and adjust for bias, study participants were initially classified by three variables—age (three categories, 50–64, 65–74 and ≥75), gender (male, female) and education (three categories, primary/none, secondary and tertiary/higher), resulting in a total of 18 (3×2×3) sample subgroups. Comparison of numbers in these subgroups, with what would be expected from the corresponding data for the population of ROI (available from the Central Statistics Office, Dublin),[15] revealed significant discrepancies. For instance, female, third-level educated and younger subjects were over-represented in the sample. However, before developing sample weights to adjust for these discrepancies, we first used logistic regression to investigate the relationship between AMD prevalence and these three variables jointly. As only the age variable was significantly related to AMD in the regression analysis, sample weights, adjusting for disproportionate representation, were calculated using just this (age) variable. These weights were then applied in all calculations of overall AMD prevalence.

The relationship between the prevalence of AMD, and established or putative risk factors for this condition, other than age, was investigated by logistic regression. Each such investigation controlled for age and included an age*risk factor interaction term. In reporting results, however, we elected to stratify by age and report prevalence with respect to potential risk factors within each age group. The 5% level of statistical significance was applied throughout all risk factor analyses, without adjustment for multiple testing.

RESULTS

Demographic characteristics of the TILDA participants studied as part of this investigation are reported in table 1. Participants with ungradable photographs were significantly older and had poorer visual acuity compared with participants with gradable photographs.

Intragrader reliability showed moderate agreement for all categories.[16] Kappa and weighted kappa scores varied from 0.51 to 0.61 and 0.60 to 0.61, respectively. Exact agreement for AMD features varied from 91% to 96%.

Prevalence of AMD

Increasing age was the only variable exhibiting a statistically significant association with AMD (defined as any AMD yes/no) in a logistic regression model including the variables age, gender and education. The development of sample weights based on this age variable is presented in table 2. The age group ≥75 constitutes over 18% of the over 50s in the Irish population, but only 8.5% of the sample reported herein. Therefore, ignoring this under-representation in the sample of the oldest age group would lead to an underestimate of prevalence of AMD. The weights (final column of table 2) adjust for this: every subject aged ≥75 in the sample is treated (in estimating overall prevalence) as representing 544 subjects in the population, whereas sample subjects in the other two age groups are treated as representative of about 225 subjects in the population.

Table 3 shows the prevalence of each category of AMD, as well as the estimated prevalence of AMD (all forms) for those aged 50 years or older in ROI. These estimates are based on the weights presented in table 2. Adjusting for age, the prevalence of AMD (any form) was 7.2% (95% CI 6.5% to 7.9%); the prevalence of early AMD was 6.6% (95% CI 5.9% to 7.3%); the prevalence of late AMD was 0.6% (95% CI 0.4% to 0.8%); the prevalence of atrophic AMD was 0.3% (95% CI 0.1% to 0.5%) and the prevalence of neovascular AMD was 0.3% (95% CI 0.1% to 0.5%).

Analysis of AMD by other demographic subgroups, stratifying by age, is shown in table 4. The p values displayed in table 4 were obtained from the χ^2 test for contingency tables. Some differences in prevalence of AMD are evident in table 4 with

Table 1 Demographic and other characteristics of TILDA baseline (wave 1) participants included in study analyses

Characteristic	Mean±SD
Age	61.61±8.10
BMI	28.42±4.51
VA	0.06±0.18
Characteristic	**n (%)**
Gender	
Male	2169 (45.7)
Female	2582 (54.3)
Total	4751 (100)
Education	
Primary/none	1013 (21.3)
Secondary	1986 (41.8)
Tertiary/higher	1750 (36.8)
Total	4749 (100)
Location	
Dublin	1383 (29.1)
Other urban	1259 (26.5)
Rural	2104 (44.3)
Total	4746 (100)
Smoking	
Never	2189 (46.1)
Past	1856 (39.1)
Current	706 (14.9)
Total	4751 (100)
Family history	
No/don't know	4496 (94.6)
Yes	255 (5.4)
Total	4751 (100)
Cardiovascular disease	
No	2987 (62.7)
Yes	1771 (37.3)
Total	4751 (100)
Stroke	
No	4690 (98.7)
Yes	61 (1.3)
Total	4751 (100)

Interval data presented as mean±SD. Categorical data presented as percentages. Cardiovascular disease refers to participants who reported no self-reported doctor's diagnosis of any of the following: angina, heart attack, heart failure, stroke, transient ischaemic attack and heart murmur. Stroke refers to participants who reported a doctor's diagnosis of stroke.
Age, age in years; BMI, body mass index (kg/m^2); Dublin, residence in Dublin city or county; Other urban, residence in other urban, another town or city in the Republic of Ireland; education, level of education; family history, subjects who reported a family history of age-related macular degeneration (AMD)—family history was defined as having a first-degree relative, that is, parent or sibling with AMD; location, location of residence in the Republic of Ireland; primary/none, subjects who did not have education and those with only primary education; rural, residence in rural area in the Republic of Ireland; secondary, subjects who completed a junior certificate or leaving certificate or equivalent; smoking, smoking status of subjects classified as never (no reported history of smoking), past (past smokers) and current (current smokers); tertiary, subjects who completed a diploma, first degree or higher degree; TILDA, the Irish Longitudinal study on Ageing; VA, visual acuity; visual acuity recorded in logarithm of the minimum angle of resolution (logMAR)—visual acuity was measured in both eyes using an Early Treatment Diabetic Retinopathy Study logMAR chart at a test distance of 4 m; only eye with best visual acuity is reported.

Table 2 Sample weights for analysis

Age group	Population (%)	Sample (%)	Weight
50–64	700 800 (58.4)	3093 (65.1)	226.6
65–74	280 900 (23.4)	1256 (26.4)	223.6
≥75	218 700 (18.2)	402 (8.5)	544.0

Weights developed from age variable. Population data were based on the Republic of Ireland population census 2011.

respect to gender, education and geographic location ('Dublin' vs 'other urban' vs 'rural'). However, a statistically significant difference was observed only for early AMD with respect to geographic location (with prevalence values of 10.8%, 18.4% and 6.3% of participants categorised as 'Dublin', 'other urban' and 'rural', respectively). Some other, statistically non-significant, findings in table 4 may be attributable to the small sample sizes of the respective subgroups; for example, prevalence of (any and early) AMD is clearly greater for women than for men in the ≥75 age group.

The prevalence of drusen within demographic subgroups, stratifying by age, is reported in table 5.

Risk factors for (any) AMD

Each risk factor for AMD (as listed in table 1) was investigated separately via logistic regression models containing that risk factor; each such model also included age, and the interaction of age with that risk factor. The dependent variable in these analyses was any AMD (yes/no); logistic analyses for smaller categories of AMD were deemed statistically infeasible. Subjects with ungradable photographs, and subjects unsure of family history for AMD, were omitted from all regression analyses.

Age was highly statistically significant in all logistic regression analyses ($p<0.005$ in all analyses). Family history was also statistically significant (OR=0.28, 95% CI for OR=0.11 to 0.69, $p=0.006$), but the age*family history interaction was not ($p=0.17$). None of the other risk factors analysed (gender, education, geographic location, body mass index (BMI), stroke, cardiovascular disease, smoking), nor their respective interactions with the age risk factor, were statistically significant ($p>0.05$ for all). For example, we obtained $p=0.10$ for BMI and $p=0.16$ for the interaction term, $p=0.44$ for cardiovascular disease and $p=0.76$ for the interaction, $p=0.32$ for stroke and $p=0.38$ for the interaction.

We considered that the other risk factors merited further exploration, beyond the basic regression findings, and that the best way to do this was to stratify by age and analyse each risk factor separately within each age group. Table 4 (first three age columns) contains this information for any AMD, and for each of the three demographic risk factors (gender, education, location). The p values displayed in table 4 were obtained from the χ^2 test for contingency tables; all p values exceed 0.05 and so support the earlier findings from the logistic regression analyses.

Positive family history was defined as having a first-degree relative, that is, parent or sibling, with AMD. The relationship of family history to (any) AMD, stratifying by age, is presented in table 6. The prevalence of AMD was significantly higher in those who reported a positive family history in the age group 65–74 (14.5% with AMD, $p=0.017$) and ≥75 (33.3% with AMD, $p=0.002$). These significant findings support the earlier findings from the logistic regression analysis.

The remaining risk factor (smoking) was not significantly associated with (any) AMD, after controlling for age ($p=0.59$ for smoking, $p=0.44$ for the interaction, in the logistic regression). Nevertheless, we have included some details of the smoking–AMD relationship in table 6. While not statistically significant, it is worth noting that in all three age groups, in table 6, prevalence of (any) AMD was higher for current smokers than for either of the other smoking groups. It is also worth reporting that, in the case of neovascular AMD (consistently associated with smoking in the literature), six of nine study subjects (67%) with this condition are past or current smokers, whereas just 54% of the TILDA sample are past or current smokers.

Other results

While logistic regression was not considered feasible for risk factor analysis for the rarer forms of AMD, table 4 has some interesting contingency table results for these. A statistically significant difference was observed for early AMD with respect to geographic location (with prevalence values of 10.8%, 18.4% and 6.3% of participants categorised as 'Dublin', 'other urban' and 'rural', respectively). Some other, statistically non-significant, findings in table 4 may be attributable to the small sample sizes of the respective subgroups; for example, prevalence of any AMD (and also early AMD) is clearly greater for women than for men in the ≥75 age group.

The prevalence of drusen within demographic subgroups, stratifying by age, is reported in table 5. There are three statistically significant results highlighted in table 5, but in general, definitive conclusions based on table 5 results (as in tables 4 and 6) are problematic because of the small numbers of subjects in certain subgroups.

DISCUSSION

This study was undertaken to investigate the prevalence of AMD in ROI using the TILDA wave 1 (baseline) sample. Subjects were randomly selected from the ROI population and therefore representative of the community-dwelling population

Table 3 Prevalence of age-related macular degeneration (AMD) by age category

Age groups (years)	Any AMD n (%)	Early AMD n (%)	Late AMD n (%)	Atrophic AMD n (%)	Neovascular AMD n (%)	Mixed AMD* n (%)
50–64	156 (5.0)	152 (4.9)	4 (0.1)	1 (0.0)	3 (0.1)	0 (0.0)
65–74	98 (7.8)	92 (7.3)	6 (0.5)	3 (0.2)	2 (0.2)	1 (0.1)
≥75	53 (13.2)	44 (11.0)	9 (2.2)	5 (1.3)	4 (1.0)	0 (0.0)
Overall unweighted	307 (6.5)	288 (6.1)	19 (0.4)	9 (0.2)	9 (0.2)	1 (0.0)
Overall weighted	86 095 (7.2)	78 950 (6.6)	7144 (0.6)	3618 (0.3)	3303 (0.3)	224 (0.0)
95% CI (overall weighted)	6.5 to 7.9	5.9 to 7.3	0.4 to 0.8	0.1 to 0.5	0.1 to 0.5	–

*Mixed AMD—subject has neovascular AMD in one eye and atrophic AMD in the other eye.

Table 4 Prevalence of age-related macular degeneration (AMD) by demographic subgroups, stratified by age group

Characteristic, n (%)	Any AMD Age groups			Early AMD Age groups			Late AMD Age groups			Atrophic AMD Age groups			Neovascular AMD Age groups		
	50–64	65–74	≥75	50–64	65–74	≥75	50–64	65–74	≥75	50–64	65–74	≥75	50–64	65–74	≥75
Gender															
Male	71 (5.2)	47 (7.8)	21 (11.1)	70 (5.1)	44 (7.3)	16 (8.4)	1 (0.1)	3 (0.5)	5 (2.6)	0 (0.0)	2 (0.3)	3 (1.6)	1 (0.1)	1 (0.2)	2 (1.1)
Female	85 (4.9)	51 (7.9)	32 (15.3)	82 (4.8)	48 (7.4)	28 (13.4)	3 (0.2)	3 (0.5)	4 (1.9)	1 (0.1)	1 (0.2)	2 (1.0)	2 (0.1)	1 (0.2)	2 (1.0)
p Value	0.771	0.947	0.211	0.672	0.927	0.113	0.435	0.933	0.630	0.372	0.524	0.577	0.700	0.961	0.924
Education															
Primary/none	28 (5.7)	34 (8.5)	15 (12.0)	27 (5.5)	33 (8.3)	9 (7.2)	1 (0.2)	1 (0.3)	6 (4.8)	0 (0.0)	0 (0.0)	3 (2.4)	1 (0.2)	1 (0.3)	3 (2.4)
Secondary	72 (5.2)	30 (6.9)	21 (13.8)	69 (4.9)	27 (6.2)	19 (12.5)	3 (0.2)	3 (0.7)	2 (1.3)	1 (0.1)	1 (0.2)	1 (0.7)	2 (0.1)	1 (0.2)	1 (0.7)
Tertiary	56 (4.6)	34 (8.1)	17 (14.2)	56 (4.6)	32 (7.6)	16 (13.3)	0 (0.0)	2 (0.5)	1 (0.8)	0 (0.0)	2 (0.5)	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)
p Value	0.628	0.658	0.863	0.744	0.501	0.242	0.277	0.656	0.069	0.545	0.377	0.382	0.356	0.603	0.147
Location															
Dublin	33 (4.0)	27 (7.0)	21 (13.3)	33 (4.0)	24 (6.2)	17 (10.8)	0 (0.0)	3 (0.8)	4 (2.5)	0 (0.0)	1 (0.3)	2 (1.3)	0 (0.0)	2 (0.5)	2 (1.3)
Other urban	48 (4.9)	27 (7.8)	18 (18.4)	46 (5.6)	26 (7.5)	18 (18.4)	2 (0.2)	1 (0.3)	0 (0.0)	1 (0.1)	1 (0.3)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
Rural	75 (5.2)	43 (8.3)	14 (9.8)	73 (5.1)	41 (7.9)	9 (6.3)	2 (0.1)	2 (0.4)	5 (3.5)	0 (0.0)	1 (0.2)	3 (2.1)	2 (0.1)	0 (0.0)	2 (1.4)
p Value	0.185	0.776	0.156	0.264	0.618	**0.013**	0.379	0.584	0.191	0.248	0.955	0.355	0.569	0.106	0.515

Level of significance set at $p<0.05$; statistical significance tested with χ^2 test for contingency tables.
Bold signifies statistically significant p value.
Dublin, residence in Dublin city or county; Other urban, residence in other urban, another town or city in the Republic of Ireland; education, level of education; location, location of residence in the Republic of Ireland; primary/none, subjects who did not have education and those with only primary education; rural, residence in rural area in the Republic of Ireland; secondary, subjects who completed a junior certificate or leaving certificate or equivalent; tertiary, subjects who completed a diploma, first degree or higher degree.

aged 50 years or older. The prevalence of AMD (any form) in ROI is estimated at 7.2%, after adjusting for different non-response rates (and different attendance rates at the health centres) in different age groups.

The prevalence estimates (and all other results presented in this paper) were obtained from subjects with gradable photographs only. Including the 108 ungradable subjects, and assuming these have the same prevalence rates within age groups as the gradable subjects, leads to some changes in AMD sample numbers within each age group, but also to changes in weights. The net effect is an overall age-adjusted estimate of 7.17% for any AMD, that is, practically identical to the estimate from the gradable subjects only.

Different population-based studies reporting prevalence estimates of AMD have adopted various photography/grading protocols and definitions for AMD. Table 7 provides AMD prevalence estimates from other studies for comparison with estimates from our TILDA study. Some large differences in reported AMD prevalence are evident in table 7 and could be either attributable to differences between the populations studied or to differences in study design (eg, grading techniques, photography protocols, sampling and recruitment strategies and age range of sample). A recent meta-analysis of the prevalence of AMD in populations of European ancestry found substantial variability in prevalence rates between studies, with differences in late AMD primarily due to differences in age profile and study design.[22] For the purpose of emphasising the important role of such variables on published findings, it is noteworthy that the prevalence of early AMD was as high as 52.3% and 58.6% in the Greenland Inuit Eye Study[23] and Prevalence of Age-related Macular Degeneration in Italy study,[24] respectively. However, in our study, we estimate the prevalence of early AMD in ROI to be 6.6%, consistent with many reports of ethnically comparable populations (eg, National Health and Nutrition Examination Survey (NHANES) 2005–2008 US population:[11] 5.7%).

The prevalence of late AMD in the current study was 0.6%, consistent with some previous reports (eg, NHANES 2005–2008 US population:[11] 0.8%; Visual Impairment Project:[25] 0.68%) but less than that reported by others (eg, Beaver Dam Eye Study:[18] 1.6%; Rotterdam Study:[12] 1.7%). However, the prevalence of neovascular AMD and atrophic AMD is known to vary between studies. In our study, we report prevalence for each of the two forms of late AMD (atrophic and neovascular) to be equal (at 0.3% each), whereas some previous studies have reported the atrophic form to be more common than the neovascular form (eg, Reykjavik Eye Study:[20] atrophic 3.2%, neovascular 0.7%). In contrast, however, the neovascular form of AMD has been reported to be more prevalent than the atrophic form of the condition in many other studies (eg, Beaver Dam Eye Study:[18] atrophic 0.6%, neovascular 1.2%; Blue Mountains Eye Study:[19] atrophic 0.7%, neovascular 1.3%; Rotterdam Study:[12] atrophic 0.6%, neovascular 1.1%; European Eye Study:[26] atrophic 1.2%, neovascular 2.3%).

In general, we found that differences in prevalence of AMD between demographic subgroups were not statistically significant, after controlling for age (tables 4 and 5). However, especially for the rarer forms of AMD, these findings are based on small cell frequencies and should be treated circumspectly.

For both men and women in this study, the impact of age on prevalence appears much stronger for the more severe forms of the disease. For example, in table 4, the prevalence of late AMD in the ≥75 age group (at 2.6%) is 5.2 times the prevalence observed for the 60–74 age group for men and 3.8 times the

Table 5 Prevalence of drusen by demographic subgroups, stratified by age group

	Hard drusen (<63 μm)* Age groups			Soft drusen (>125 μm) Age groups		
Characteristic, n (%)	50–64	65–74	≥75	50–64	65–74	≥75
Gender						
Male	36 (2.6)	15 (2.5)	2 (1.1)	34 (2.5)	29 (4.8)	14 (7.4)
Female	49 (2.9)	20 (3.1)	9 (4.3)	33 (1.9)	28 (4.3)	19 (9.1)
p Value	0.702	0.515	**0.047**	0.289	0.688	0.533
Education						
Primary/none	18 (3.7)	13 (3.3)	4 (3.2)	9 (1.8)	20 (5.0)	5 (4.0)
Secondary	40 (2.9)	11 (2.5)	4 (2.6)	29 (2.1)	16 (3.7)	15 (9.9)
Tertiary	27 (2.2)	11 (2.6)	3 (2.5)	29 (2.4)	21 (5.0)	13 (10.8)
p Value	0.240	0.789	0.938	0.735	0.559	0.104
Location						
Dublin	23 (2.8)	10 (2.6)	3 (1.9)	10 (1.2)	14 (3.6)	14 (8.9)
Other urban	21 (2.6)	11 (3.2)	5 (5.1)	25 (3.1)	15 (4.3)	13 (13.3)
Rural	41 (2.9)	13 (2.5)	3 (2.1)	32 (2.2)	28 (5.4)	6 (4.2)
p Value	0.929	0.816	0.262	**0.033**	0.445	**0.040**

Level of significance set at p<0.05; statistical significance tested with χ^2 test for contingency tables.
Bold signifies statistically significant p value.
*More than 10 hard drusen (<63 μm).
Dublin, residence in Dublin city or county; Other urban, residence in other urban, another town or city in the Republic of Ireland; education, level of education; location, location of residence in the Republic of Ireland; primary/none, subjects who did not have education and those with only primary education; rural, residence in rural area in the Republic of Ireland; secondary, subjects who completed a junior certificate or leaving certificate or equivalent; tertiary, subjects who completed a diploma, first degree or higher degree.

observed prevalence for women. In contrast, for early AMD, the corresponding risk ratios are 1.2 and 1.8 for men and women, respectively. Similarly, in table 5, prevalence of soft drusen in the ≥75 group is 1.5 times and 2.1 times the prevalence observed in the 60–74 group for men and women, respectively, whereas the corresponding risk ratios for hard drusen are just 0.4 and 1.4 for men and women, respectively.

While primarily concerned with the prevalence of AMD, we also investigated possible associations with this condition, especially for variables that have been previously identified as risk factors for AMD. In this regard, we report that the prevalence of AMD increases with increasing age, consistent with all other studies.[18 19] Also, family history for AMD was strongly associated with prevalence of this condition, consistent with other studies.[27 28] In fact, in the 65–74 and ≥75 age groups, the prevalence of AMD is strikingly greater for subjects who reported a family history of this condition. Self-reported data with respect to family history for AMD are problematic for the following reasons: reporting of AMD among siblings is subject to influence by the number of siblings; reporting of AMD among parents is subject to influence by the longevity of those parents; reporting of AMD among participants who were adopted will be irrelevant with respect to a genetic predisposition for AMD; and finally, reporting of early AMD is likely to be under-represented because it is typically asymptomatic. Nevertheless, and with full appreciation of these limitations, and given that we excluded subjects who replied that they did not know whether or not a first-degree relative suffered from AMD, we believe that our findings that self-reported family history of AMD is a risk factor for the condition are important.

Table 6 Risk factors for prevalence of age-related macular degeneration (AMD), stratified by age group

	Any AMD Age groups		
Characteristic, n (%)	50–64	65–74	≥75
Smoking			
Never	77 (5.4)	39 (6.7)	24 (13.0)
Past	50 (4.4)	44 (8.5)	25 (13.1)
Current	29 (5.5)	15 (10.1)	4 (16.7)
p Value	0.420	0.290	0.881
Family history			
No	134 (5.0)	75 (7.2)	40 (11.7)
Yes	9 (6.1)	12 (14.5)	8 (33.3)
p Value	0.564	**0.017**	**0.002**

Level of significance set at p<0.05; statistical significance tested with χ^2 test for contingency tables.
Bold signifies statistically significant p value.
Family history, subjects who reported a family history of AMD—family history was defined as having a first-degree relative, that is, parent or sibling with AMD; smoking, smoking status of subjects classified as never (no reported history of smoking), past (past smokers) and current (current smokers).

However, with respect to other potential risk factors for which no statistically significant associations with AMD were observed in the current study, it should be appreciated that controlling for age in the logistic regression analyses, and stratifying AMD prevalence by age group, may have contributed to the non-identification of some potentially significant associations with AMD.

The strengths of our study include (1) the use of a population-representative cohort of subjects aged 50 years and older in ROI; (2) the study population is racially homogeneous, over 99% being white; and (3) retinal photographs were graded in a masked fashion using standard protocols by the same person and therefore reducing intergrader variability. The large sample size (nearly 5000) could also be considered a strength, but the need to stratify by age group meant that, for some analyses, subgroup sizes were small.

The limitations of this study include the use of monoscopic retinal photographs through undilated pupils, rendering it difficult to obtain quality photographs in the presence of significant media opacities. The TILDA investigators elected to use monoscopic retinal photographs in the study because other health

Table 7 Prevalence of age-related macular degeneration (AMD) in comparable population-based studies

Study name	Country	Age group (year)	Early AMD (%)	Late AMD (%)	Atrophic AMD (%)	Neovascular AMD (%)
Baltimore Eye Survey*	USA	40–49		0.0	0.0	0.0
1985–1988[17]		50–59		0.5	0.2	0.4
		60–69		0.7	0.7	0.0
		70–79		2.9	1.8	1.6
		80+		7.0	4.0	5.6
Beaver Dam Eye Study	USA	43–54	8.4	0.1		
1988–1990[18]		55–64	13.8	0.6		
		65–74	18.0	1.4		
		75+	29.7	7.1		
Blue Mountains Eye Study	Australia	49–54	1.3	0.0		
1992–1993[19]		55–64	2.6	0.2		
		65–74	8.5	0.7		
		75–84	15.5	5.4		
		85+	28.0	18.5		
Reykjavik Eye Study	Iceland	50–59	8.9	0.3	0.3	0.0
1996[20]		60–69	16.4	1.2	1.2	0.0
		70–79	27.5	5.8	5.3	0.5
		>80	37.1	30.8	25.0	9.8
MESA*	USA	45–54	1.8	0.0		
2000–2002[21]		55–64	2.8	0.1		
		65–74	5.5	0.3		
		75–84	13.3	2.9		
TILDA Study	ROI	50–64	4.9	0.1	0.1	0.1
2009–2011		65–74	7.3	0.5	0.2	0.2
		≥75	11.0	2.2	1.3	1.0

*Data on only white participants.
MESA, Multi-ethnic Study of Atherosclerosis; ROI, Republic of Ireland; TILDA, the Irish Longitudinal Study on Ageing.

assessment measures (eg, gait) were to be conducted immediately following retinal photography, and the results of such tests would have been influenced and confounded by pharmacological pupillary dilation. Also, subjects with ungradable images were more likely to be older and have poor vision, although (upon investigation) this did not appear to have much effect on our prevalence estimates.

The response rate in the TILDA study (62% of eligible households participated) is in line with other national household surveys of older people, for example, in the Survey of Health, Ageing and Retirement in Europe, the average response rate across all countries was 55%.[29] Moreover, a non-response rate of this magnitude had been anticipated (from pilot surveys prior to the main survey) and built into the sample size calculations for the TILDA study. However, non-attendance at health centres reduced the effective participation rate further, so that just 5035 of 8175 participants (61.6%), who were successfully enrolled in the broader TILDA study, actually took part in this AMD study; this represents just 38% of the individuals originally selected. This has to be acknowledged as a weakness of our study, although we were able to adjust our prevalence calculations, to take account of the distorted sample age structure that arose from this non-participation. Of note, while many of the studies listed in table 7 reported much higher response rates than our AMD study (eg, 83.1% for the Beaver Dam Study), most of these were not nationally representative population-based studies and are not directly comparable.

In conclusion, this study reports the prevalence of AMD in ROI for the first time and will inform healthcare providers and planners involved in the delivery of care to those suffering with this condition.

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Prevalence of age-related macular degeneration in the Republic of Ireland

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