Global prevalence of age-related macular degeneration and disease burden projection for 2020 and 2040: a systematic review and meta-analysis

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Summary

Background Numerous population-based studies of age-related macular degeneration have been reported around the world, with the results of some studies suggesting racial or ethnic differences in disease prevalence. Integrating these resources to provide summarised data to establish worldwide prevalence and to project the number of people with age-related macular degeneration from 2020 to 2040 would be a useful guide for global strategies.

Methods We did a systematic literature review to identify all population-based studies of age-related macular degeneration published before May, 2013. Only studies using retinal photographs and standardised grading classifications (the Wisconsin age-related maculopathy grading system, the international classification for age-related macular degeneration, or the Rotterdam staging system) were included. Hierarchical Bayesian approaches were used to estimate the pooled prevalence, the 95% credible intervals (CrI), and to examine the difference in prevalence by ethnicity (European, African, Hispanic, Asian) and region (Africa, Asia, Europe, Latin America and the Caribbean, North America, and Oceania). UN World Population Prospects were used to project the number of people affected in 2014 and 2040. Bayes factor was calculated as a measure of statistical evidence, with a score above three indicating substantial evidence.

Findings Analysis of 129 664 individuals (aged 30–97 years), with 12 727 cases from 39 studies, showed the pooled prevalence (mapped to an age range of 45–85 years) of early, late, and any age-related macular degeneration to be 8·01% (95% CrI 3·98–15·49), 0·37% (0·18–0·77), and 8·69% (4·26–17·40), respectively. We found a higher prevalence of early and any age-related macular degeneration in Europeans than in Asians (early: 11·2% *vs* 6·8%, Bayes factor 3·9; any: 12·3% *vs* 7·4%, Bayes factor 4·3), and early, late, and any age-related macular degeneration to be more prevalent in Europeans than in Africans (early: 11·2% *vs* 7·1%, Bayes factor 12·2; late: 0·5% *vs* 0·3%, 3·7; any: 12·3% *vs* 7·5%, 31·3). There was no difference in prevalence between Asians and Africans (all Bayes factors <1). Europeans had a higher prevalence of geographic atrophy subtype (1·11%, 95% CrI 0·53–2·08) than Africans (0·14%, 0·04–0·45), Asians (0·21%, 0·04–0·87), and Hispanics (0·16%, 0·05–0·46). Between geographical regions, cases of early and any age-related macular degeneration were less prevalent in Asia than in Europe and North America (early: 6·3% *vs* 14.3% and 12·8% [Bayes factor 2·3 and 7·6]; any: 6·9% *vs* 18·3% and 14·3% [3·0 and 3·8]). No significant gender effect was noted in prevalence (Bayes factor <1·0). The projected number of people with age-related macular degeneration in 2020 is 196 million (95% CrI 140–261), increasing to 288 million in 2040 (205–399).

Interpretation These estimates indicate the substantial global burden of age-related macular degeneration. Summarised data provide information for understanding the effect of the condition and provide data towards designing eye-care strategies and health services around the world.

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Introduction

Age-related macular degeneration accounts for 8·7% of all blindness worldwide and is the most common cause of blindness in developed countries,[1–5] particularly in people older than 60 years. Its prevalence is likely to increase as a consequence of exponential population ageing. There have been significant advances in the management of exudative or so-called wet age-related macular degeneration with the introduction of anti-angiogenesis therapy, and patients now have effective treatment options that can prevent blindness and, in many cases, restore vision.[6–10] However, these treatments are expensive and not available to all patients in many countries.[11–14] Thus, understanding the prevalence, burden, and population impact is essential for adequate health care planning and provision, which require both precise and contemporary estimates of disease prevalence.

Although there have been many population-based studies of age-related macular degeneration around the world, there are no summarised data to guide global strategies. Furthermore, studies have suggested substantial racial or ethnic differences in disease prevalence. In the Baltimore Eye Study, people of European (white) ancestry were more likely to have early and late-stage disease than were those of African

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ancestry.[15,16] Two meta-analyses done in populations of European[17] and Asian ancestry[4] suggest that, in people aged 40–79 years, the age-specific prevalence of late age-related macular degeneration in Asians (0·56%) was similar to that in Europeans (0·59%), but early signs were less common in Asians (6·8%) than in Europeans (8·8%). No studies had systematically compared the prevalence of the condition across geographical regions.

To address this gap, we did a systematic review of the literature to estimate the prevalence of age-related macular degeneration, and assess differences by ethnicity, region, and sex, and to project the number of individuals affected worldwide by the condition in 2020 and 2040.

Methods

Search strategy

We systematically reviewed publications that reported prevalence of age-related macular degeneration by searching the electronic databases of PubMed, Web of Science, and Embase for relevant papers published up to May, 2013, with the following search terms (formatted for PubMed search): ("Macular Degeneration"[Mesh] AND ("Prevalence"[Mesh] OR "Epidemiology"[Mesh] OR "Cross-Sectional Studies" [Mesh] OR "Cohort Studies"[Mesh])); (("age-related maculopathy"[All Fields] OR "age-related maculopathy"[All Fields] OR "age-related macular degeneration"[All Fields] OR "age related macular degeneration"[All Fields] OR "macular degeneration"[All Fields]) AND ("prevalence"[All Fields] OR "incidence"[All Fields] OR "epidemiology"[All Fields] OR "risk factors"[All Fields])).

The strategy identified all articles used in previous reviews.[4,17] Reference lists of identified reports were also scanned to identify other relevant studies. The initial search was scrutinised in detail by clinician scientist XS and reviewed by senior clinician scientist C-YC. Data were checked by statisticians (WLW, XL). Disagreements were resolved by discussion.

Inclusion and exclusion criteria

Our meta-analysis was done according to the Meta-analysis Of Observational Studies in Epidemiology (MOOSE) guidelines.[18] The full texts of potentially relevant articles were reviewed to identify studies that met the inclusion and exclusion criteria. The two criteria for inclusion were: a population-based study from a defined geographic area; and a standardised photographic assessment of age-related macular degeneration.

Population-based studies were included if they quantified the prevalence (including early, late, and exudative or neovascular age-related macular degeneration, and geographic atrophy) in population-based samples, with clearly defined methods of sampling. A response rate of 50% or higher was considered adequate for inclusion,[19] with the exception of the European Eye Study (EUREYE) study[20] since it was a large population study (45%); sensitivity analysis showed almost no effect on our robust model estimates (appendix p 9). Surveys or audits of hospital eye departments or clinics were excluded. Studies inviting non-specific volunteers or particular professions were excluded, as were studies that relied on self-reported diagnoses or did fundus examinations only in those with reduced vision.

For the standardised photographic assessment, we included studies that had used retinal photography and standardised grading methods to diagnose and classify lesions (ie, grading of retinal photographs following either the Wisconsin age-related maculopathy grading system,[21] the international classification for age-related macular degeneration,[22] or the Rotterdam staging system[23]) with reproducible grading results.

Studies fulfilling any one of the following were excluded: use of only clinical examination by ophthalmoscopy or slit-lamp biomicroscopy for diagnosis (ie, lack of any grading reproducibility assessment); reports of number of eyes with age-related macular degeneration as opposed to the number of individuals; studies in which determination of prevalence was not one of the primary study objectives (eg, studies determining risk factors); and studies not population-based, but were interview-based or audits of hospital eye departments. Although we did not specifically exclude non-English literature, the studies included in the final analysis were all in English.

The classification systems used to define those with early, late, and any age-related macular degeneration (geographic atrophy and neovascular age-related macular degeneration) in each study were recorded with the Wisconsin age-related maculopathy grading system[21] or the international classification.[22] Early disease was defined as either any soft drusen (distinct or indistinct) and pigmentary abnormalities or large soft drusen 125 μm or more in diameter with a large drusen area (>500 μm diameter circle) or large soft indistinct drusen in the absence of signs of late-stage disease. Late age-related macular degeneration was defined as the presence of any of the following: geographic atrophy or pigment epithelial detachment, subretinal haemorrhage or visible subretinal new vessel, or subretinal fibrous scar or laser treatment scar.

Statistical analysis

Because intrinsic difficulties exist when undertaking a meta-analysis of data from varied studies with differing characteristics such as disease definition, age distribution of the sample, and prevalence estimates stratified by age and sex versus single prevalence estimates, we constructed statistical models to best describe and fit our extracted data. Heterogeneity issues were addressed in our pooled meta-analysis using a hierarchical Bayesian approach to establish the worldwide prevalence of age-related macular degeneration. This approach models the hierarchical