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Equity reporting in systematic reviews and meta-analysis for geographic atrophy: a PROGRESS-Plus assessment

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Abstract

Context: As systematic reviews and meta-analyses (SRMAs) are crucial for treatment development, they must provide guidelines that represent diverse patient demographics to promote equitable health care. As new research and treatment modalities are being developed for geographic atrophy (GA), establishing an equitable research foundation is becoming vitally important to physicians as they personalize their treatment plans.

Objectives: This analysis aims to determine whether SRMAs pertaining to GA are reporting equity-related items utilizing the PROGRESS-Plus framework.

Methods: We conducted a cross-sectional analysis by searching databases for systematic reviews and meta-analyses concerning GA from the year 2000 to November 2023. From this search, 176 articles returned, but only 57 of them met all the inclusion criteria. After screening the articles for inclusion, data pertaining to PROGRESS-Plus items were extracted. All analyses were conducted in a masked and duplicative fashion. χ^2 tests were employed to determine whether associations existed between the variables.

Results: From the initial search, 176 articles returned, of which 119 were excluded due to duplication, data unrelated to GA, or because it was animal-based research. Of the remaining 57 studies, 26 (45.6 %) included zero PROGRESS-

Plus items. Fewer articles from the US-reported equity items (31.3 %, 5/16) compared to other countries (63.4 %, 26/41), which held statistical significance ($p=0.028$).

Conclusions: The American Academy of Ophthalmology has created initiatives to increase diversity, equity, and inclusion within the subspecialty. By using the PROGRESS-Plus framework, this study concluded that the majority of the articles pertaining to GA do not meet equity item objectives. As these documents aid physicians in developing treatment plans, these findings are concerning as physicians may find it more difficult to individually tailor treatment plans according to each patient's holistic needs. Limitations in this study included unintentional omission or misclassification of research documents despite the comprehensive search string and double-blinded analysis. Furthermore, the results of this study cannot be generalized to other areas of research.

Keywords: age-related macular degeneration; cross-sectional analysis; equity; geographic atrophy; ophthalmology; PROGRESS-Plus

In developed countries such as the United States, Australia, Japan, and much of Western Europe, age-related macular degeneration (ARMD) is the leading cause of registered legal blindness in individuals older than 65 [1]. In 2019, it was estimated by the Centers for Disease Control and Prevention (CDC) that 19.8 million Americans are living with the disease [2]. As ARMD progresses, there is a greater risk of developing either the neovascular form or geographic atrophy (GA), both of which are vision-threatening late sequelae. GA, in particular, is an irreversible and centrally blinding manifestation characterized by sharply demarcated hypopigmented lesions that usually appear first in the perifoveal macula [3]. Over time, these lesions will likely expand into areas of drusen, or whitish-yellow deposits within the retina, and eventually into the fovea [4]. Reticular pseudodrusen, a particular subtype of drusen located above the retinal pigment epithelium (RPE), has been more closely associated with GA development and

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multilobular atrophy expansion [3–6]. Visualization of atrophic lesions can be done by a fundus examination or other imaging modalities. On optical coherence tomography (OCT), GA is identified by RPE atrophy and light hypertransmission through the retinal layers, whereas on fundus autofluorescence (FAF), these lesions appear as hypofluorescent patches due to their lack of lipofuscin [3, 6]. The size and growth of GA can also be monitored with regular examinations and imaging, FAF being particularly recommended for this purpose in the literature [5]. The rates of GA expansion are highly correlated with the age of disease onset, as those diagnosed at a younger age are likely to have a poorer prognosis [5]. As atrophy progresses into the fovea, visual acuity is significantly decreased due to the development of irreversible central scotomas [7].

Several factors play a role in the advancing size and progression of GA. Increasing age and a family history of the disease magnify the risk of developing this sequela [7–9]. A predilection based on gender is still debated in the literature. Although some articles suggest that this may be a male-predominant disease, other studies have found no statistical significance between males and females [8, 9]. Among different ethnic populations, it has been shown that those of European or Native American ancestry are more likely to develop GA, whereas the Asian population is less likely to do so [8, 10].

Modifiable risk factors for GA include smoking and hypercholesterolemia [11, 12]. Smoking has proven to increase the risk of disease onset as well as hasten lesion growth once present, whereas quitting has demonstrated the ability to decrease GA development [7, 13]. While research has shown that eating low-glycemic-index foods such as those found in the Mediterranean diet can protect against GA enlargement [14, 15], individuals experiencing *food insecurity* – defined by the United States Department of Agriculture as “a household-level economic and social condition of limited or uncertain access to adequate food” – are less likely to be able to obtain these foods, and they are not able to afford antioxidant vitamins that have shown to slow moderate ARMD progression before the disease progresses to later stages such as GA [4, 16]. Although a correlation between physical activity and progression to late-stage ARMD has been debated in the literature, overall incidence of the disease has proven to be lower among individuals with higher physical activity levels [17, 18]. Other conditions, such as diabetes or cardiovascular disease, are associated with ARMD because many risk factors for all three diagnoses are the same [19]. Altogether, the current research hypothesis is that all of these factors alter complement and mitochondrial function, increasing or mitigating oxidative stress and contributing to disease pathogenesis or prevention [20].

Systematic reviews and meta-analyses (SRMAs) that address GA and disease epidemiology are of utmost importance to physicians when developing treatment plans. These documents summarize the most recent literature and are frequently used as a starting point for disease management [21]. With this in mind, creating SRMAs that apply to all populations is crucial because they can promote equitable care by providing more information to the doctors who read them. Equitable care, in turn, may lead to decreased disease burden. These facts have not been overlooked by the American Academy of Ophthalmology (AAO), which predicted that creating an environment that reduces disparities may significantly reduce the projected growth of visual impairments and blindness in the United States by the year 2050 [22, 23]. To take this one step further, the AAO has created a task force that produces commentaries and publications that highlight how social determinants such as education, healthcare accessibility, health literacy, and even ZIP code can have a significant impact on the care given to patients and their visual outcomes [22]. As these initiatives are underway, it remains unclear whether the literature utilized to manage GA reflects this hard work directed toward increasing equity.

A framework commonly utilized to assess equitable reporting in SRMAs is called *PROGRESS*. It was developed by Evans and Brown in 2003 and is a method by which to analyze literature and draw conclusions regarding its holistic reporting or lack thereof [24, 25]. The acronym *PROGRESS* stands for Place of residence, Race/ethnicity/culture/language, Occupation, Gender/sex, Religion, Education, Socioeconomic status, and Social capital [24]. The original framework was modified to *PROGRESS-Plus* – allowing additional categories including personal characteristics associated with discrimination (e.g., age, disability), features of relationships (e.g., smoking parents, excluded from school, smoking in the home), and time-dependent relationships (e.g., leaving the hospital, respite care, other instances where a person may be temporarily at a disadvantage), etc. [25, 26] For this study, we employed the *PROGRESS-Plus* method to analyze SRMAs concerning GA, because it is unknown whether the current literature comprehensively addresses all social determinants of health. We hypothesize that a majority of SRMAs pertaining to GA do not adequately report equity-related items found in this framework. Given the detrimental effects of GA to patients' vision and the many new treatment advancements being made specifically for it, it is important to have an equitable research foundation for further advancement. By analyzing this, we hope to provide more insight to those researching and treating GA, as well as to potentially reduce the predicted future disease burden.

Methods

Search criteria and eligibility

This study adhered to methodology for conducting meta-epidemiologic research established by Murad and Wang [27]. In November 2023, we conducted a systematic search of PubMed (MEDLINE), Embase, and Cochrane databases from the year 2000 to the time of our query. Our search string in PubMed included (“Geographic Atrophy” [Mesh] OR “geographic atrophy”) AND (“Meta-Analysis” [Publication Type] OR “Systematic Review” [Publication Type]), in Embase was (‘geographic atrophy’/exp OR ‘geographic atrophy’) AND (‘systematic review’/exp OR ‘review, systematic’ OR ‘systematic review’ OR ‘meta analysis’/exp OR ‘analysis, meta’ OR ‘meta analysis’ OR ‘meta-analysis’ OR ‘meta-analysis’) AND ([article]/lim OR [article in press]/lim OR [review]/lim), and in the Cochrane database, “geographic atrophy” in title abstract or keyword was utilized. We did not restrict our search by language; however, no studies returned that were in any language other than English. After utilizing this search string, each SRMA that appeared was examined by two researchers (RE and DS) in a masked, duplicative fashion utilizing the Rayyan Stata 16.1 software to see whether the documents reported data on GA and if they focused on human research. Studies that focused broadly on ARMD or its neovascular form were not included in this study because those studies did not publish data specifically on GA. Papers that contained animal data were likewise excluded. Once both researchers examined the SRMAs, any disagreements on eligibility were resolved through discussion with a third author (MH), who acted as an arbiter until 100 % agreement was reached.

Equity assessment and data extraction

To determine whether equitable reporting was taking place in the eligible literature, a form containing PROGRESS-Plus criteria was completed for each SRMA. On this form, it was noted whether any of the PROGRESS items were present in the SRMA as well as what we captured as *plus* items including age, disability, smoking status, presence of others smoking in the household, diet/food security, physical activity level, and other comorbidities that were present or absent in these SRMAs. All SRMAs were evaluated this way by two other researchers (TM and HR), also in a masked and duplicative manner. Other data that were extracted included the residing country of the first author, affiliations of the first author, funding source of the article, number of primary

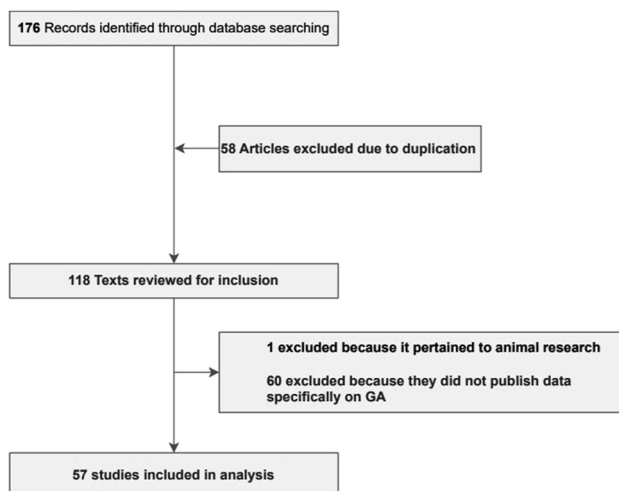


Figure 1: A PRISMA flow diagram showing the breakdown of the screening process with reasons for exclusion.

studies included, overall sample size, presence or absence of patient-reported outcome measures, and whether the article mentioned PROGRESS or PRISMA-equity (Preferred Reporting Items for Systematic Reviews and Meta-Analyses). After completing this analysis, the data were reconciled by the first two researchers, who discussed the conflicting answers and reanalyzed the texts.

Data analysis

First, we reported the number of articles returned from the initial search string, the number of studies excluded, and the reason for exclusion. Next, we reported the frequency of SRMAs, including any equity components from the PROGRESS-Plus items, and the frequency of each item. Finally, we assessed the associations of the article components listed above with the presence of PROGRESS-Plus items utilizing chi-squared tests. Statistical analyses were conducted in Stata 16.1 (StataCorp, LLC, College Station, TX) with alpha set at 0.05. This study was submitted for ethics review to the Oklahoma State University Center for Health Sciences’ Institutional Review Board (IRB) and was determined to be nonhuman subjects research.

Results

Our initial search string yielded 176 articles, of which 119 were excluded because they were duplicates or did not meet the eligibility criteria. Figure 1 is a PRISMA flow diagram that

Table 1: The frequency of PROGRESS-Plus items included within systematic reviews (n=57).

PROGRESS-Plus item inclusion	No., %
0	26 (45.61)
1	11 (19.3)
2	3 (5.26)
3	5 (8.77)
4	7 (12.28)
5	2 (3.51)
6	1 (1.75)
7	1 (1.75)
8	0 (0)
9	0 (0)
10	1 (1.75)

shows the breakdown of the screening process with the reasons for exclusion.

All of the data from the search string and analysis have been uploaded to Open Science Framework and can be viewed with the following link: https://osf.io/hbafm/?view_only=928da914008d4f74aaa5e1a9cb2e53d2.

Equity inclusion within systematic reviews

Of the 57 SRMAs included in our sample, 31 (55.4 %) included at least one element of the PROGRESS framework with age, sex, and gender most widely distributed – leaving 26 (45.6 %) articles that did not include any PROGRESS-Plus items (Table 1). An additional 26 articles contained less than five of the extracted elements but named at least one. Only 4 (7.0 %) articles contained 5–9 items, and only one (1.8 %) contained 10 items (Table 1). The most commonly cited constituents were age, which was listed in 43.9 % of analyzed SRMAs, gender/sex (29.8 %), and race/ethnicity (28.1 %) (Table 2). Smoking status was listed in 7 (12.3 %) SRMAs, and nutritional status/food security was listed in 2 (3.5 %) (Table 2). Religion and the presence of others smoking in the household were not cited in any article, and occupation, socioeconomic status (SES), social capital, education, disability, and a sedentary lifestyle were only listed in one SRMA (Table 2).

Additional study characteristics

Among the study characteristics that were extracted alongside PROGRESS-Plus items, the location of the study was the only one found to be statistically significant ($p=0.03$). Of the 31 SRMAs that contained at least one PROGRESS-Plus item, 26 of them were conducted outside of the United States

Table 2: Systematic reviews' inclusion of PROGRESS-Plus items (n=57).

PROGRESS-Plus item inclusion	No., %
Place	14 (24.56)
Race/ethnicity	16 (28.07)
Occupation	1 (1.75)
Gender/sex	17 (29.82)
Religion	0 (0)
Education	1 (1.75)
Socioeconomic status, SES	1 (1.75)
Social capital	1 (1.75)
Age	25 (43.86)
Disability	1 (1.75)
Smoking status	7 (12.28)
Others smoking in HH	0 (0)
Food security/nutritional status	2 (3.51)
Sedentary lifestyle	1 (1.75)
Other comorbidities	6 (10.53)

HH, health history.

(Table 3). Over two-thirds (68.8 %) of the SRMAs conducted within the United States did not contain any PROGRESS-Plus elements, compared to 36.6 % in non-US countries. First-author affiliations, study funding, presence of patient-reported outcome measures, and specifically mentioning PRISMA-equity or PROGRESS within the articles were not found to be statistically significant (Table 3).

Discussion

In summation, our study found that a vast majority of PROGRESS-Plus items were under-reported in SRMAs about GA. Certain demographics such as age, gender/sex, and race/ethnicity were more likely to be named in the literature than others. Religion, education, SES, etc., may not have been listed as often due to a lack of data collection for the review or within the primary trials that were being reviewed. Also, the perceived relevance of these items in relation to diagnosis and disease management may not be as great as the demographics that were reported more frequently. One particular study confirmed these hypotheses by devising a questionnaire to determine how many physicians discussed religious preferences with their patients and what their attitudes were toward the query itself [28]. They found that roughly 50 % of doctors who responded regularly documented a patient's religion and that physician comfort level and perception of its importance were both statistically associated with that percentage [28]. This may or may not be true of other underreported PROGRESS items that are not as readily available or gathered by healthcare workers before patient encounters.

Table 3: Associations between inclusion of any PROGRESS-Plus items and study characteristics.

	Does not include any PROGRESS-Plus items No., %	Include PROGRESS-Plus items No., %	χ^2, P
Total	26 (45.61)	31 (54.39)	–
Location of study			
Non-United States	15 (36.59)	26 (63.41)	4.80,
United States	11 (68.75)	5 (31.25)	0.028
Affiliation of first author			
Government or gov- ernment agency	0 (0)	1 (100)	6.05, 0.11
Hospital or medical institution	4 (23.53)	13 (76.47)	
Industry	1 (50)	1 (50)	
University	21 (56.76)	16 (43.24)	
Funding for study			
Government or gov- ernment agency	4 (25)	12 (75)	4.92, 0.30
Hospital, medical institution	3 (37.5)	5 (62.5)	
Industry	6 (54.55)	5 (45.45)	
No funding	3 (60)	2 (40)	
Not available	10 (58.82)	7 (41.18)	
Mentions PRISMA-Equity or PROGRESS framework within article			
No	25 (48.08)	27 (51.92)	1.45,
Yes	1 (20)	4 (80)	0.23
Did the SR include any patient-reported outcomes as assessment measures?			
No	23 (46)	27 (54)	0.02,
Yes	3 (42.86)	4 (57.14)	0.88

PRISMA, preferred reporting items for systematic reviews and meta-analyses; SR, systematic review.

Although these results highlight disparities within SRMAs pertaining to GA, these trends are consistent with other research. Previous meta-epidemiologic research using the PROGRESS-Plus framework in the fields of pain medicine [29] and maternal and childbirth outcomes during the COVID-19 pandemic [30] also had similar trends; in pain medicine, age was the most commonly reported item among these SRMAs, while in maternal and childbirth, location was the most commonly reported item. More broadly, a scoping review analyzed equity-relevant papers in all fields of study and found that even in those documents, age and sex/gender were reported most frequently, whereas religion was reported the least of all PROGRESS items [31]. Another paper looked at equity-relevant randomized control trials to determine whether PROGRESS items were being accounted for in separate subgroup analyses. They subsequently discovered that no trial accounted for place of residence, occupation, religion, education, or social capital [32]. Thus, equity reporting in SRMAs pertaining to GA should address

these gaps, but it is in line with other fields of research. Therefore, individuals conducting SRMAs on GA, as well as in other fields, should adopt an equity-based framework that guides the research in addressing each of these items – especially when cultural sensitivity is warranted to achieve optimal health outcomes. Journal editors could include requirements for systematic reviews to include an equity checklist in combination with the PRISMA checklist that is often required for submitting a manuscript.

Limitations

Limitations of this study include the potential for missing SRMAs in the initial search of databases, even though we used comprehensive search strings. Additionally, although two experienced reviewers screened all articles for inclusion independently, there is potential for misclassification and exclusion of SRMAs during the initial assessment. Because this study strictly pertains to SRMAs reporting data about GA, it cannot be generalized to other ophthalmic literature; however, this specifically speaks to the need for SRMAs in this field to expand the literature in order to be more inclusive of these measures. Furthermore, there is the potential for review-level insufficiencies due to under-reporting, because SRMAs can only reflect what is said in primary studies. Lastly, some research has shown that although the PROGRESS-Plus model does analyze many of the sociodemographic factors affecting one's health, it does not necessarily analyze "relationships between various concepts that may lead to inequality/inequity." [33] Because there is no current framework built to analyze these relationships, future research could be performed to address this deficit.

Conclusions

ARMD continues to be the leading cause of legal blindness among individuals 65 years and older in developed countries worldwide [34]. GA in particular, even though it is currently a disease entity of much research and therapeutic development, continues to be a more devastating sequela because the damage it produces is entirely irreversible [3]. The widespread ramifications of this disease highlight the importance of both clinical research and continuing education for health practitioners. The literature produced and utilized by clinicians must not only contain the most current treatment guidelines, but also include patients of all demographics so that their practice can be more individually and holistically tailored. In this study, we discovered that

nearly half of the SRMAs about GA omitted all PROGRESS-Plus items. Although some demographics such as age, sex/gender, and race/ethnicity were more frequently reported, others such as socioeconomic status and education were often neglected. Ensuring that our literature provides data for diverse populations becomes crucial because it can increase equitable care, allow for a more holistic and osteopathic approach to treatment, and mitigate disease burden for patients.

Research ethics: The Oklahoma State University Institutional Review Board determined this study to be non-human subjects research (IRB #2024183). It adhered to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines.

Informed consent: Not applicable.

Author contributions: The authors have accepted responsibility for the entire content of this manuscript and approved its submission.

Use of Large Language Models, AI and Machine Learning Tools: None declared.

Conflict of interest: None declared.

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Data availability: This study used data from the Cochrane (<https://www.cochranelibrary.com>), Embase (<https://www.embase.com/search/quick>), and PubMed (<https://pubmed.ncbi.nlm.nih.gov>) databases, which are publicly available data sources.

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