Table 1. Meta-analysis of Observational Studies in Epidemiology Checklist[1]

Item No	Criteria	Brief description of how the criteria were handled in the meta-analysis
Reporting of background should include		
1	Problem definition	What is the progression pattern and growth rate of unifocal and multifocal geographic atrophy (GA) secondary to non-exudative age-related macular degeneration?
2	Hypothesis statement	Unifocal and multifocal GA have the same progression pattern but distinct growth rates.
3	Description of study outcome(s)	The growth rate of GA lesions' area (in mm^2/year) and the growth rate of GA lesions' effective radius ($\frac{1}{\sqrt{\pi}} \times \sqrt{GA\ area}$) in mm/year.
4	Type of exposure or intervention used	Untreated eyes with GA secondary to nonexudative AMD.
5	Type of study designs used	Not limited to any study type.
6	Study population	Patients diagnosed of GA secondary to nonexudative AMD in at least one eye without any treatment intended to slow or halt the atrophy progression.
Reporting of search strategy should include		
7	Qualifications of searchers (e.g., librarians and investigators)	The librarian (Grossetta Nardini, Holly) who created the searches has a master's degree and 20 years of experience as a medical librarian and expert literature database searcher.
8	Search strategy, including time period included in the synthesis and key words	Reported in Supplementary Method (available at http://www.ophthalmology-retina.org). No limitation by time period/date(s).
9	Effort to include all available studies, including contact with authors	We searched multiple databases for thoroughness and screened all articles meeting the inclusion criteria. We contacted the corresponding authors of primary studies that did not report crucial data for our meta-analysis.
10	Databases and registries searched	MEDLINE, EMBASE, Cochrane Library (Wiley), clinicaltrials.gov, and NLM PubMed
11	Search software used, name and version, including special features used (e.g., explosion)	Ovid interface for MEDLINE and Embase. MeSH terms (controlled vocabulary), adjacency, explosion, and textwords were all used.
12	Use of hand searching (e.g., reference lists of obtained articles)	The reference list of all included articles were further confirmed through hand search.
13	List of citations located and those excluded, including justification	The list is included in Table 4, available at http://www.ophthalmology-retina.org.
14	Method of addressing articles published in languages other than English	English abstracts were located for all foreign language articles. After screening, no pertinent articles not in English remained.
15	Method of handling abstracts and unpublished studies	Unpublished studies and/or conference abstracts without full text were not included.
16	Description of any contact with authors	We contacted the corresponding authors of studies that did not report crucial data for our meta-analysis.
17	Description of relevance or appropriateness of studies assembled for assessing the hypothesis to be tested	Detailed inclusion criteria were described in the methods section

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Reporting of methods should include		
18	Rationale for the selection and coding of data (e.g., sound clinical principles or convenience)	Studies were included as per inclusion criteria. Study selection was independently performed by at least two reviewers. Two reviewers (L.L.S., M.S.) independently extracted the data from each study and the data were relevant to the population characteristics, study design, exposure, and outcome.
19	Documentation of how data were classified and coded (e.g., multiple raters, blinding and interrater reliability)	After data extraction of individual study by M.S. and L.L.S., the two reviewers reviewed the data together. Disparities were resolved through discussion.
20	Assessment of confounding (e.g., comparability of cases and controls in studies where appropriate)	Two investigators assessed confounding factors in each study with the Quality In Prognosis Studies (QUIPS) tool. We also analyze the impact of different study designs and imaging modalities on the GA effective radius growth rate.
21	Assessment of study quality, including blinding of quality assessors, stratification or regression on possible predictors of study results	Two investigators (L.L.S. and M.S.) evaluated the quality of each study using the Quality In Prognosis Studies (QUIPS) tool. The QUIPS tool was suggested by the Cochrane Collaboration and allowed us to assess the risk of bias of prognosis studies in 6 bias domains: study participation, study attrition, prognostic factor measurement, outcome measurement, study confounding, and analysis and reporting (Table 2, available at http://www.ophthalmology-retina.org).
22	Assessment of heterogeneity	Heterogeneity was assessed with the I^2 index.
23	Description of statistical methods (e.g., complete description of fixed or random effects models, justification of whether the chosen models account for predictors of study results, dose-response models, or cumulative meta-analysis) in sufficient detail to be replicated	Described in the methods section.
24	Provision of appropriate tables and graphics	We included the Preferred reporting items for systematic reviews and meta-analyses flow-chart and several tables to describe the literature search and its results. Several figures were used to describe the main findings of the analyses and findings.
25	Graphic summarizing individual study estimates and overall estimate	Figure 5. Figure 4 and 6 (available at http://www.ophthalmology-retina.org)
26	Table giving descriptive information for each study included	Table 3.

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Reporting of results should include		
27	Results of sensitivity testing (e.g., subgroup analysis)	Sensitivity analysis was undertaken by removing one study each time to repeat the random-effects meta-analyses. No single study affected the statistical significance in the difference of GA growth rate between unifocal and multifocal groups. No single study significantly affected the GA effective radius growth rate in unifocal or multifocal GA group.
28	Indication of statistical uncertainty of findings	The mean estimates and errors for the outcome have been reported in the text, figures, and tables.
Reporting of discussion should include		
29	Quantitative assessment of bias (e.g., publication bias)	Two investigators (L.L.S. and M.S.) evaluated the quality of each study using the Quality In Prognosis Studies (QUIPS) tool. We evaluated the publication bias using the funnel plots and Egger test.
30	Justification for exclusion (e.g., exclusion of non-English language citations)	The list is included in Table 4 (available at http://www.ophthalmology-retina.org).
31	Assessment of quality of included studies	Two investigators (L.L.S. and M.S.) evaluated the quality of each study using the Quality In Prognosis Studies (QUIPS) tool. The grading for each study is in Table 5 (available at http://www.ophthalmology-retina.org).
Reporting of conclusions should include		
32	Consideration of alternative explanations for observed results	We propose that the growth rate of GA area (regardless of the number of lesions in the eye) is directly proportional to the total perimeter, which is a measure of the number of RPE cells exposed at the border of the atrophic lesions. One alternative hypothesis is that multifocal GA represents a more advanced stage of GA compared to unifocal GA. This could be the case if eyes with multifocal GA may have more extensive subretinal drusenoid deposits, worse local environments (e.g., micronutrient deficiency or hypoxia), and/or different proportions of RPE cells with distinct fates including migratory or apoptotic compared to eyes with unifocal GA.
33	Generalization of the conclusions (ie, appropriate for the data presented and within the domain of the literature review)	This meta-analysis demonstrated that the effective radius of GA enlarges linearly as a function of time in both unifocal and multifocal groups. The growth rate of GA effective radius or square root of area measured by 3 imaging modalities (CFP, FAF, and OCT) is comparable and can serve as a reliable outcome measure to monitor the progression of both unifocal and multifocal GA. The growth rate of multifocal GA was 1.46-folds higher than the growth rate of unifocal GA (slightly > $\sqrt{2}$). We propose that the growth rate of GA area (regardless of the number of lesions in the eye) is directly proportional to the total perimeter, which is a measure of the number of RPE cells exposed at the border of the atrophic lesions.
34	Guidelines for future research	The total perimeter of GA lesions should be considered during the assessment of the severity and prognosis of GA. Additional studies are needed to understand the cellular mechanisms underlying this relationship.
35	Disclosure of funding source	Research reported in this publication was supported by the National Institute on Aging of the National Institutes of Health under Award Number T35AG049685. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health.

Reference:

1. Stroup DF, Berlin JA, Morton SC, et al. Meta-analysis of observational studies in epidemiology: a proposal for reporting. JAMA 2000;283(15):2008-12.