Protocol of global incidence and progression of age-related macular degeneration
A systematic review

Shan Zhao, MDa, Xiaowen Lan, BMb, Jingyang Wu, MMc, Song Yue, MMc, Han Zhang, PhDc, Qiang Wu, MMd, Guisen Zhang, MMd, Lei Liu, PhDc,∗

Abstract

Background: There have been many reports on the prevalence and incidence of age-related macular degeneration (AMD), and there are some systematic reviews reporting on the pooled prevalence of AMD. However, there is no systematic review of incidence or progression of AMD worldwide. Given the few evidences regarding the pooled incidence or progression of AMD, we performed this meta-analysis protocol to investigate the global incidence or progression of AMD. In addition, we will investigate the risk factors for AMD incidence or progression using meta-analysis.

Methods: Four English databases (PubMed, EMBASE, Cochrane Library, and Web of Science) and four Chinese databases (CMB, CNKI, VIP, and Wanfang database) will be searched to identify relevant studies. The primary outcome of this meta-analysis is the incidence or progression of AMD. The second outcome of this meta-analysis is risk factors for the incidence or progression of AMD. Meta-analysis was performed to calculate the pooled incidence or progression rate and 95% confidence interval of AMD. Pooled risk ratios of risk factors (age, gender, smoking, and hypertension) for AMD incidence or progression were computed as the Mantel–Haenszel-weighted average of the risk ratios for all included studies. Sensitivity analysis, subgroup analysis, quality assessment, and publication bias analysis will be performed to ensure the reliability of our findings.

Results: This study will provide a current evidence of global pooled incidence or progression of AMD. Further, current study will provide evidence-based risk factors for AMD incidence or progression. Moreover, our study will project the incident number of people with AMD from 2030 to 2050.

Conclusion: This systematic review and meta-analysis will provide evidence to develop major public health strategies for preventing AMD. Ethics and dissemination: ethical approval is not required because our systematic review and meta-analysis will be based on published data without interventions on patients. The findings of this study will be published in a peer-reviewed journal.

Abbreviations: AMD = age-related macular degeneration, PRISMA = Preferred Reporting Items for Systematic Reviews and Meta-Analyses.

Keywords: age-related macular degeneration, burden, incidence, meta-analysis, progression

1. Introduction

With the increasing numbers of people living longer, the number of people with age-related diseases is rising worldwide. Age-related macular degeneration (AMD) is a common age-related disease which is also a leading cause of visual impairment and severe vision loss.[1] To date, prevalence of AMD is likely to increase due to exponential population ageing.[2] There have been some studies on the incidence and prevalence of AMD, with systemic reviews summarizing global estimates of its prevalence across regions.[3] Moreover, there is 1 report on late-AMD incidence among American Whites[4] which showed annual incidence of late AMD was 3.5 per 1000 aged ≥50 years. In particular, there is no systematic review of incidence or progression of AMD worldwide and little is known about the incidence and progression of early stage of AMD and the disease in other parts of population apart from American Whites. Furthermore, interpreting incidence estimates from different studies on the incidence of AMD is challenging because of significant variation in its estimates between ethnicities and regions, due to differences in study setting, method of ascertainment of AMD, and follow-up time trends. Robust data
on incidence and progression of AMD are important for development of major public health strategies to prevent this disease.

To address this gap, we conducted a systematic review and meta-analysis to estimate the global incidence or progression of AMD, and to describe variations by ethnicity, region, study characteristics, and follow-up time period in which the studies were conducted.

2. Methods

2.1. Design and reporting

This systematic review will be designed according to the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) guidelines. For current protocol, the PRISMA statement for Protocols (PRISMA-P) was used for its description (Table 1). This systematic review is registered in the PROSPERO International Prospective Register of systematic reviews with number CRD42019118832.

2.2. Data source and search strategy

Published primary studies will be gathered using four English databases (PubMed, EMBASE, Cochrane Library, and Web of Science) and four Chinese databases (CMB, CNKI, VIP, and Wanfang database). References of the relevant articles will be searched by hand. Moreover, for article which is difficulty accessing sufficient data or full text, its corresponding author will be contacted by e-mail. The key search terms will be “incidence,” “development,” “associated factors,” “progression,” and “age-related macular degeneration.” Using all these terms, relevant topics will be searched through ‘All fields’ using the connecting ‘AND’ and ‘OR’ as appropriate.

2.3. Inclusion criteria

Type of studies: prospective or retrospective cohort studies.
Type of participants: population over 40 years old.
Type of outcome: incidence or progression (or studies giving enough data to compute these estimates if not directly calculated) of AMD.
Language: English or Chinese.

2.4. Exclusion criteria

Type of studies: case–control studies, cross-sectional studies, case reports, case series, letters, reviews, and editorials.
Duplicate reports.

2.5. Selection of studies for inclusion in the review

Articles will be identified by 1 clinical scientist and reviewed by another senior clinical scientist. Data will be evaluated by a statistician, and consensually retain studies to be included. Disagreements when existing will be solved by discussion.

2.6. Data extraction and management

Data will be extracted using a designed form. Two reviewers will independently extract data. The domains included study setting (title, follow-up time, design, and region), study population (age, gender, and ethnicity), method of ascertainment of AMD, and information on severity level of AMD.

2.7. Appraisal of methodological quality of included studies and risk of bias

Methodological quality for included studies will be evaluated using the 10-item rating scale (Table 2). Each item will be assigned a score of 1 (yes) or 0 (no), and each score will be summed across items to generate an overall study quality score. Included studies will be defined into 3 levels according to overall score as follows: low risk of bias (8–10), moderate risk (6–7), and high risk (0–5).

2.8. Data synthesis

Incidence of AMD was calculated as cumulative incidence including both early AMD and late AMD and any-AMD. According to included studies varied in time of follow-up, we calculated annual incidence of AMD using the formula −ln (1 − S)/t, where S is the proportion of new AMD cases over t years and t is the time of follow-up.[7] Similar to the incidence of AMD, we will calculate the cumulative progression and the annual progression estimates of AMD. We will perform subgroup analysis on the incidence of AMD by study region, population age and gender, follow-up duration, and method of ascertainment of AMD. We will also assess the effect of major risk factors for AMD incidence including age, gender, ethnicity, smoking, and others wherever data were available.

2.9. Assessment of reporting biases

The presence of publication and selective reporting bias will be assessed using symmetry of funnel plots and Egger’s test.[8] Asymmetry of the funnel plot or a P value of Egger’s regression test less than 0.05 will be considered indicative of significant publication bias.

2.10. Ethics and dissemination

Ethics approval is not required as this is a systematic review and meta-analysis using published data. We will report our findings of this systematic review and meta-analysis in a peer-reviewed journal in future.

3. Discussion

The burden of age-related diseases is increasing in China, as a common age-related eye disease, AMD is becoming a common cause of visual impairment and blindness in elder population. In this comprehensive systematic review and meta-analysis, we will include cohort studies regarding the incidence or progression of AMD worldwide. Moreover, this systematic review and meta-analysis will provide summarized data to establish global incidence or progression estimates and its risk factors. Furthermore, current systematic review and meta-analysis will project the number of people with AMD from 2030 to 2050 which will be a useful guide for public health strategies to control AMD.

Author contributions

Author contributions: L.L. developed the study protocol, S.Z. and X.W.L. developed the search strategy. J.Y.W. and S.Y. will scan the included studies. H.Z. and G.S.Z. extract the data and assess the risk of bias. L.L. will act as an arbiter if there is any disagreement in this study. L.S. and Q.W. will perform data analysis. All authors will contribute to data interpretation. S.Z.
Table 1
Table PRISMA-P (Preferred Reporting Items for Systematic review and Meta-Analysis Protocols) 2015 checklist: recommended items to address in a systematic review protocol.

| Section and topic | Item no | Checklist item | Reported on page number |
|-------------------|---------|----------------|------------------------|
| Administrative information | | | |
| Title: | 1a | Identify the report as a protocol of a systematic review | 1 |
| | 1b | If the protocol is for an update of a previous systematic review, identify as such | Na |
| | 2 | If registered, provide the name of the registry (such as PROSPERO) and registration number | 6 |
| Authors: | | | |
| Contact | 3a | Provide name, institutional affiliation, e-mail address of all protocol authors; provide physical mailing address of corresponding author | 1 |
| Contributions | 3b | Describe contributions of protocol authors and identify the guarantor of the review | 1 |
| Amendments | 4 | If the protocol represents an amendment of a previously completed or published protocol, identify as such and list changes; otherwise, state plan for documenting important protocol amendments |  |
| Support: | | | |
| Sources | 5a | Indicate sources of financial or other support for the review | 2 |
| | 5b | Provide name for the review funder and/or sponsor | 2 |
| | 5c | Describe roles of funder(s), sponsor(s), and/or institution(s), if any, in developing the protocol | 2 |
| Introduction | | | |
| Rationale | 6 | Describe the rationale for the review in the context of what is already known | 5 |
| Objectives | 7 | Provide an explicit statement of the question(s) the review will address with reference to participants, interventions, comparators, and outcomes (PICO) | 5 |
| Methods | | | |
| Eligibility criteria | 8 | Specify the study characteristics (such as PICO, study design, setting, time frame) and report characteristics (such as years considered, language, publication status) to be used as criteria for eligibility for the review | 6 |
| Information sources | 9 | Describe all intended information sources (such as electronic databases, contact with study authors, trial registers or other grey literature sources) with planned dates of coverage | 6 |
| Search strategy | 10 | Present draft of search strategy to be used for at least 1 electronic database, including planned limits, such that it could be repeated | 6 |
| Study records: | | | |
| Data management | 11a | Describe the mechanism(s) that will be used to manage records and data throughout the review | 6 |
| Selection process | 11b | State the process that will be used for selecting studies (such as 2 independent reviewers) through each phase of the review (i.e., screening, eligibility, and inclusion in meta-analysis) | 6 |
| Data collection process | 11c | Describe planned method of extracting data from reports (such as piloting forms, done independently, in duplicate), any processes for obtaining and confirming data from investigators | 6 |
| Data items | 12 | List and define all variables for which data will be sought (such as PICO items, funding sources), any unplanned data assumptions and simplifications | 6 |
| Outcomes and prioritization | 13 | List and define all outcomes for which data will be sought, including prioritization of main and additional outcomes, with rationale | 7 |
| Risk of bias in individual studies | 14 | Describe anticipated methods for assessing risk of bias of individual studies, including whether this will be done at the outcome or study level, or both; state how this information will be used in data synthesis | 7 |
| Data synthesis | 15a | Describe criteria under which study data will be quantitatively synthesized | 7 |
| | 15b | If data are appropriate for quantitative synthesis, describe planned summary measures, methods of handling data, and methods of combining data from studies, including any planned exploration of consistency (such as I², Kendall’s τ) | 7 |
| | 15c | Describe any proposed additional analyses (such as sensitivity or subgroup analyses, meta-regression) | 7 |
| Meta-bias (es) | 16 | If quantitative synthesis is not appropriate, describe the type of summary planned | 7 |
| | 17 | Specify any planned assessment of meta-bias (es) (such as publication bias across studies, selective reporting within studies) | 7 |
| Confidence in cumulative evidence | | Describe how the strength of the body of evidence will be assessed (such as GRADE) | 8 |

*It is strongly recommended that this checklist be read in conjunction with the PRISMA-P Explanation and Elaboration (cite when available) for important clarification on the items. Amendments to a review protocol should be tracked and dated. The copyright for PRISMA-P (including checklist) is held by the PRISMA-P Group and is distributed under a Creative Commons Attribution License 4.0. From: Shamseer L, Moher D, Clarke M, Ghersi D, Liberati A, Petticrew M, Shekelle P, Stewart L, PRISMA-P Group. Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015: elaboration and explanation. BMJ. 2015 Jan 2;349 (Jan02 1):g7647.
and L.L. drafted and revised the manuscript. All authors have read and approved the final version of the manuscript.

Data curation: Xiaowen Lan.
Investigation: Jingyang Wu.
Methodology: Shan Zhao, Song Yue, Guisen Zhang.
Project administration: Han Zhang.
Software: Song Yue.
Supervision: Lei Liu.
Validation: Lei Liu.
Writing – original draft: Shan Zhao, Xiaowen Lan, Han Zhang, Qiang Wu, Guisen Zhang, Lei Liu.
Writing – review & editing: Shan Zhao, Guisen Zhang, Lei Liu.

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