PROGNOSTIC FACTORS FOR AGE-RELATED MACULAR DEGENERATION: AN OVERVIEW OF SYSTEMATIC REVIEWS

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INTRODUCTION

- Age-related macular degeneration (AMD) is the leading cause of irreversible vision loss among older adults worldwide.
- Numerous studies have identified potential prognostic factors for AMD progression, but findings are often inconsistent.
- This overview synthesizes evidence from existing systematic reviews to identify and assess the most consistently reported prognostic factors for AMD.

Objective:
To summarize and evaluate prognostic factors (PFs) associated with the progression of AMD.

Data source and methods:
- Searched a database of 8,875 systematic reviews curated by Cochrane Eyes and Vision (CEV), covering PubMed, Embase, and the Cochrane.
- Used Covidence to extract review characteristics and associations between PFs and AMD progression.
- Assessed the methodological reliability of each review using a CEV-developed tool for clinical and guideline development.
- Extracted reported risk of bias assessments for the primary studies included in each review.

RESULTS

- Seventeen systematic reviews and meta-analyses met inclusion criteria, reporting 218 prognostic factors, with 79 highlighted as particularly important or prevalent.
- Factors were organized into 20 distinct types across eight categories, including ocular functional and structural markers, lifestyle behaviors, and intervention-related characteristics.
- Modifiable factors with the strongest evidence included **dietary antioxidant or multivitamin supplementation** and **smoking cessation**, both associated with slower AMD progression.
- Most PFs were non-modifiable, with **structural biomarkers** (e.g., OCT findings) most consistently linked to disease progression.
- **No reviews investigated social determinants** as PFs, and evidence for other lifestyle and intervention-related factors remained limited.

Table 1. Table of Systematic Review Characteristics

Category	Characteristic	Value
General Study Characteristics	Number of included studies (median, range)	20 (6–94)
	Number of included participants (median, range)	9,182 (379–208,056)
Countries Represented	Most common country (×3)	4 (24%), 4 (24%), 4 (24%)
	Other countries	5 (29%)
Reliability Assessment	Not reliable reviews	8 (47%)
	Reliable reviews	9 (53%)
Types of Prognostic Factors*	Demographic & social	2 (12%)
* Reviews may examine multiple different types of prognostic factors	Lifestyle	7 (41%)
	Clinical comorbidities	3 (18%)
	Intervention-related	7 (41%)
	Functional/structural biomarkers	10 (59%)
	Genetic factors	3 (18%)
Types of Analyses	Quantitative	10 (59%)
	Qualitative only	7 (41%)
Progression Outcomes Examined	GA radius growth rate	4 (24%)
	Progression of AMD or rate of progression	3 (18%)
	Progression to late AMD	2 (12%)
	Risk of worsening AMD or vision loss	1 (6%)

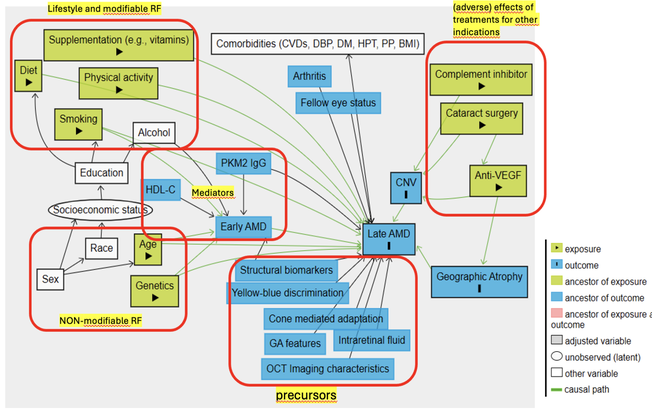

Figure 1. Directed Acyclic Graph of PFs

CONCLUSIONS

- OCT-based functional and structural biomarkers were the most consistently supported predictors of disease worsening.
- Modifiable lifestyle factors were frequently associated with progression.
- Substantial heterogeneity across reviews—definitions, methods, and follow-up durations—limits the certainty of clinical conclusions.
- Incorporating high-risk imaging features, biomarker data, and comorbidity profiles may enhance prognostic accuracy.
- Future research should investigate social, systemic, and lifestyle determinants to broaden understanding of AMD progression.

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