# INPLASY

## Status quo and outlook of polygenic risk score in ophthalmology - a protocol of systematic review

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## ADMINISTRATIVE INFORMATION

**Support -** No.

**Review Stage at time of this submission -** Completed but not published.

**Conflicts of interest -** None declared.

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**Amendments -** This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 07 February 2024 and was last updated on 07 February 2024.

## INTRODUCTION

**Review question / Objective** This study is a systematic review and focuses on ophthalmic diseases and polygenic risk score. It stresses on summarizing the application of polygenic risk score in assessing, predicting or managing ocular disorders. Also, the outlook of polygenic risk score in ophthalmology is discussed.

**Rationale** With the advent of genome-wide association study (GWAS), which is empowered by the next-generation sequencing technique, researchers are allowed to unveil the role of genes in various diseases and localize relevant mutations. Genetic risk score (GRS), a method that summed up the number of representative single nucleotide polymorphism (SNPs) in disease-associated genes with or without weighting, was developed and applied to estimate the in-born genetic risk of diseases. Furthermore, GRS was improved by electing a broader spectrum of disease-associated SNPs directly from GWAS and assigning them with different weight. And polygenic risk score (PRS) was raised. Synonymous terms, for example, polygenetic risk score, have been employed to describe identical tools. As a scale of hereditary propensity, PRS had been introduced in research in multiple disciplines, yielding promising results regarding disease prediction, outcome estimation and molecular mechanism.

Increasingly, PRS was employed in ocular diseases, ranging from common blinding diseases, including age-related macular degeneration, glaucoma and refractive errors, to rare ones. Its application brought further insight of pathogenesis of multifactorial ophthalmic disorders and allowed genetic screening of common diseases like glaucoma, myopia, and AMD. Despite promising results, its real-world utility had been questioned ophthalmologists. In a recent review focusing on

clinical application of PRS, only primary open-angle glaucoma, AMD and myopia, were discussed. More comprehensive review of PRS in a broader spectrum of ocular diseases were need.

**Condition being studied** This systematic review focuses primarily on development and application of polygenic risk score in ophthalmology. And it aims to provide an updated view of past and current works on PRS in ophthalmology and its outlook. Conditions to be studies include glaucoma, macular degeneration, myopia and other ocular disorders.

## METHODS

**Search strategy** Articles searching was conducted on four datasets, PudMed, Embase, Scopus and Web of Science, by the strings: ("genetic risk score" or "polygenic risk score" or "genetic risk scores" or "polygenic risk scores" or "polygenic scores" or "genetic scores" or "genetic score" or "polygenic score") AND (eye OR ophthalmology OR glaucoma OR myopia OR macular degeneration OR retina). All eligible literatures with at least English titles and abstracts available before or on January 1st, 2024, will be collected and imported into the software, Zotero (version 6.0.15).

**Participant or population** This study is a systematic review regarding polygenic risk score in ophthalmology and it neither includes patients from primary research directly nor conducts meta-analysis. Instead, this study includes cohort and case-control studies and results of primary research came from participants that received polygenic risk score assessment, with or without ocular disorders.

**Intervention** Not applicable. This systematic review aims at summarizing past and current works regarding polygenic risk scores and ocular disorders and it includes observational studies. No interventions are required.

**Comparator** Not applicable. This systematic review aims at summarizing past and current works regarding polygenic risk scores and ocular disorders. No comparasion was made between populations.

**Study designs to be included** This systematic review includes cohort studies and case-control studies.

**Eligibility criteria** Inclusion criteria: cohort and case-control studies that focused on both PRS and ophthalmological disorders are considered eligible for this systematic review. Exclusion criteria:(1) Either PRS or ophthalmic endpoints are missed;(2) The literature type is not research article;(3) The study design is not observational;(4) No full-text available;(5) The study is not in vivo;(6) The PRS model is not dedicated to eye diseases but to other diseases or ocular parameters;(7) PRS is not the pivot of the study;(8) Only unweighted PGS models are used;(9) Non-case-control and non-cohort studies.

**Information sources** Articles searching was conducted on four datasets, PudMed, Embase, Scopus and Web of Science.

**Main outcome(s)** Not applicable. In this systematic review, studies regarding PRS and ocular diseases are included and discussed.

**Data management** Not applicable. No meta-analysis was conducted in this study and all literatures searched were collected and stored in the software, Zotero (version 6.0.15).

**Quality assessment / Risk of bias analysis** The New-Castle Ottawa scale, which is dedicated for quality assessment of case-control and cohort studies from selection of subjects, comparability between groups, exposure, and outcome, was adopted to evaluate the included research.

**Strategy of data synthesis** Not applicable. This systematic review aims at summarizing past and current works regarding polygenic risk scores and ocular disorders. No data synthesis was conducted.

**Subgroup analysis** Not applicable. This systematic review aims at summarizing past and current works regarding polygenic risk scores and ocular disorders. No subgroup analysis was conducted.

**Sensitivity analysis** Not applicable. This systematic review aims at summarizing past and current works regarding polygenic risk scores and ocular disorders. No sensitivity analysis was conducted.

**Language restriction** English.

**Country(ies) involved** The study is carried out in China.

**Keywords** Polygenic risk score; genetic risk score; glaucoma; macular degeneration; myopia.

**Dissemination plans** This review is expected to be published and available publicly.

**Contributions of each author**
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