

Metabolomics in Primary Open Angle Glaucoma: A Systematic Review and Meta-Analysis

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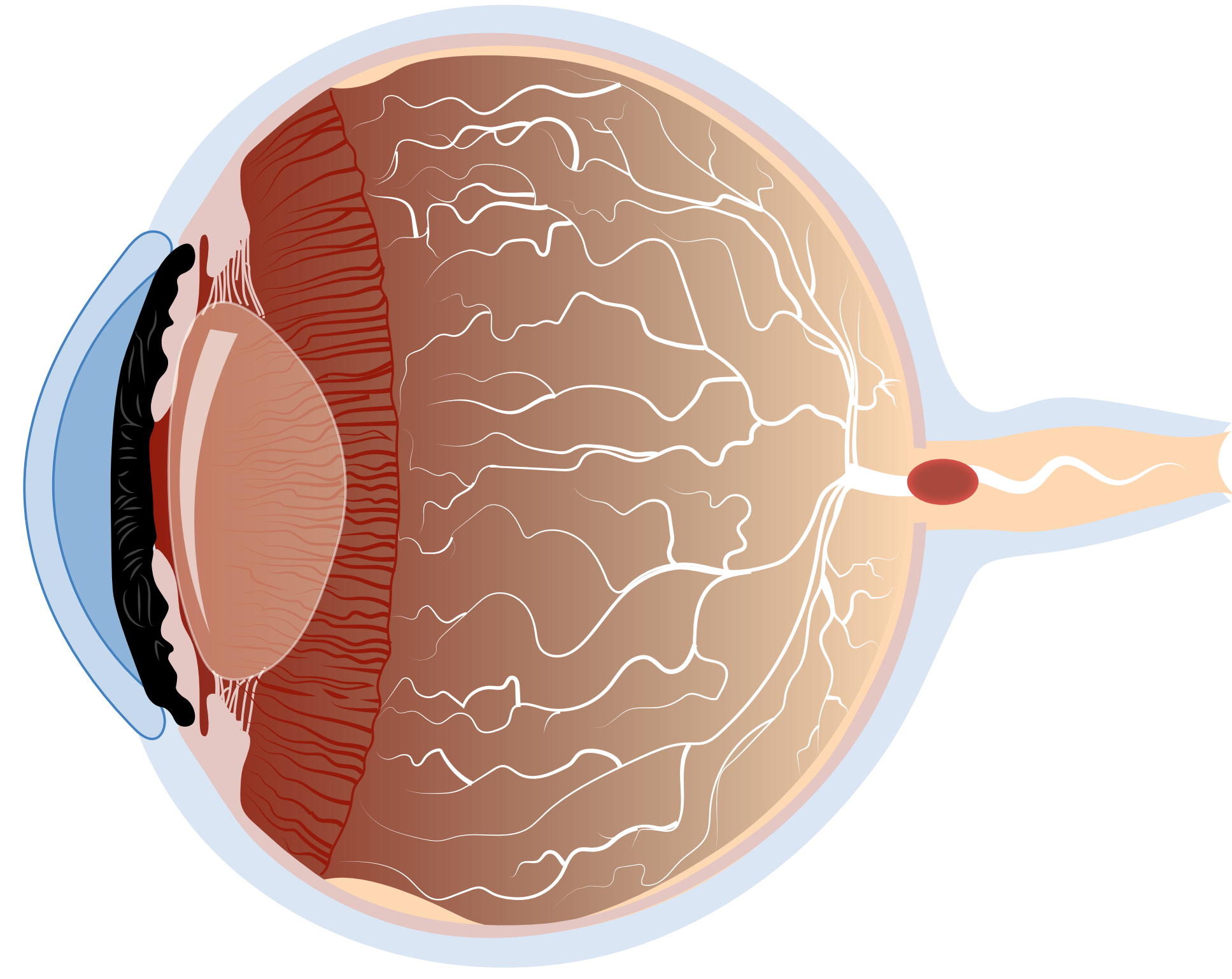
Rationale

Glaucoma affects nearly **80 million people worldwide** and this number is expected to reach 111.8 million by 2040¹

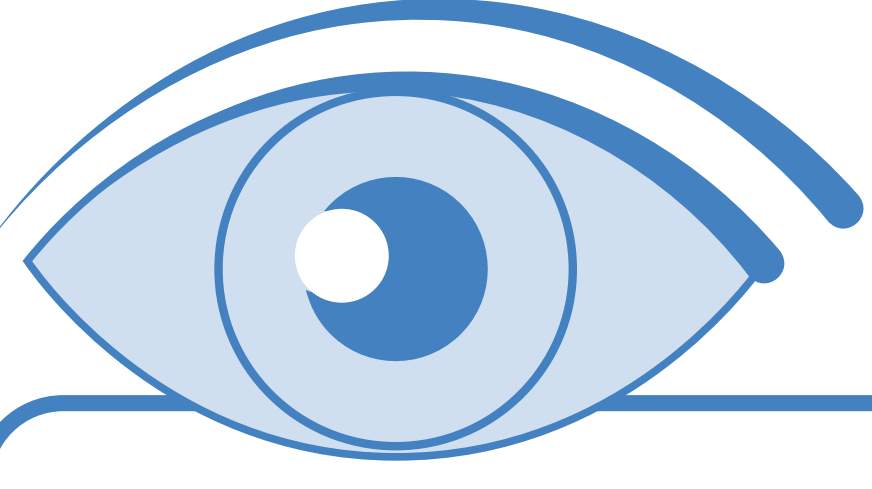
Primary open-angle glaucoma (POAG) is the most common form

Currently, patients with POAG are diagnosed based on clinical and ancillary examinations

While studies have provided insights into the metabolites present in the plasma and aqueous humour of people with glaucoma, outcomes have not been consistently validated by large sample sizes and analysis techniques



Unmet clinical need



Early diagnosis and prompt treatment to prevent permanent and irreversible visual loss

Biomarkers for early detection

Glaucoma may be associated with metabolic alterations

Metabolic profiles may potentially serve as biomarkers for early detection or as treatment targets



Aim: To perform a systematic review and meta-analysis of studies assessing the metabolomic profiles of POAG to gain further insights into disease pathogenesis

Study design

Records identified by systematic search of databases using the words 'glaucoma' and 'metabolomics' OR 'metabolomic' for studies dated up to August 2021

PubMed (n=56)

EMBASE (n=71)

Web of science (n=53)

Records after duplicates removed (n=98)

Records after screening title and abstract (n=18)

Records after full-text assessed for eligibility (n=18)

Literatures based on inclusion and exclusion criteria (n=18)

Extract data from included literatures and find overlap (n=15)

Studies included in meta-analysis (n=9)

Metabolites included in meta-analysis (n=10)

Excluded (n=80)

Literature review (n=13)

Comments (n=8)

Unrelated (n=43)

Animal (n=16)

Excluded (n=7)

No full text found (n=7)

Included (n=7)

Papers found from reference (n=7)

Systematic review and pathway enrichment

Excluded study (n=3)

No quantitative data

Excluded metabolites

Measured in less than 3 studies

Inclusion criteria

Studies focusing on POAG and analysis of the metabolites of the blood plasma or aqueous humour using nuclear magnetic resonance or liquid or gas chromatography-mass spectrometry

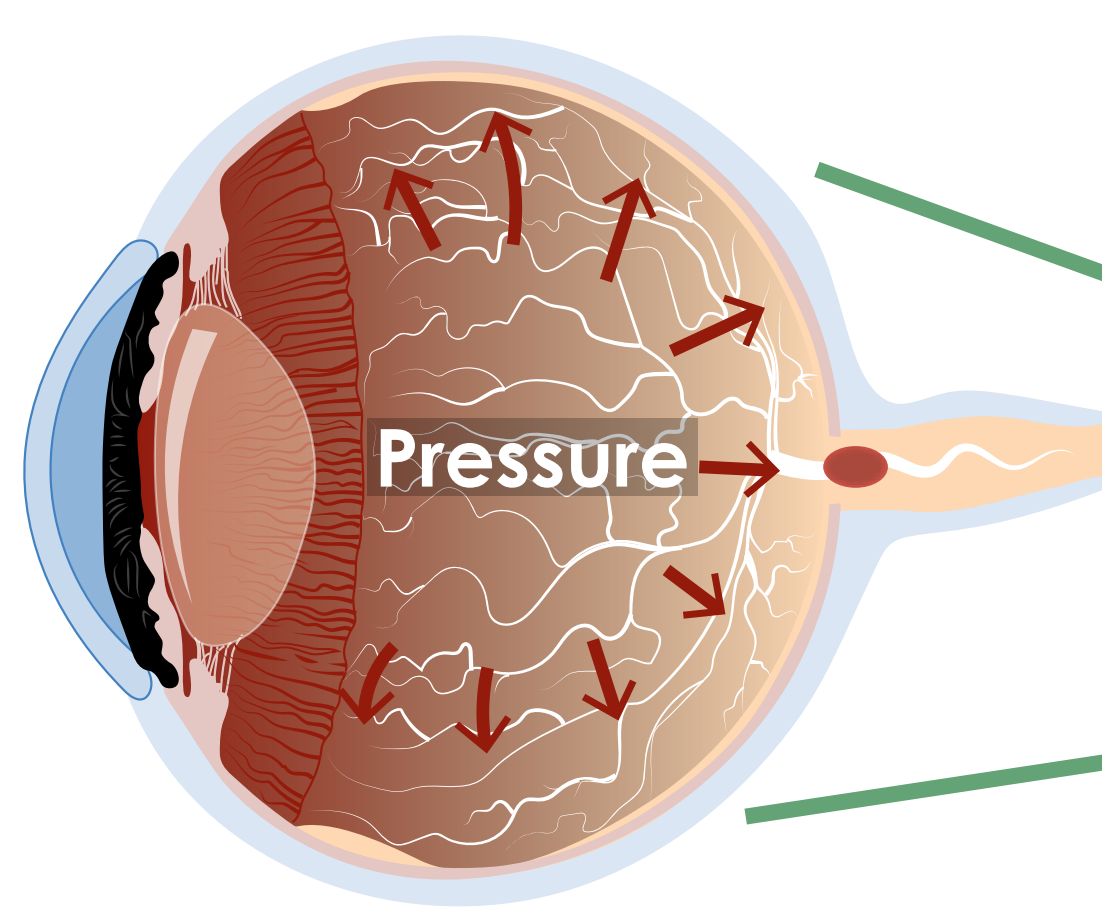
Exclusion criteria

Mouse studies or other animal models, alternative forms of glaucoma, other ocular diseases, metabolites of body fluids other than aqueous humour and blood plasma

Results and conclusion

Alanine, creatine, glycine and lysine were significantly higher in the aqueous humour of patients with POAG compared to controls

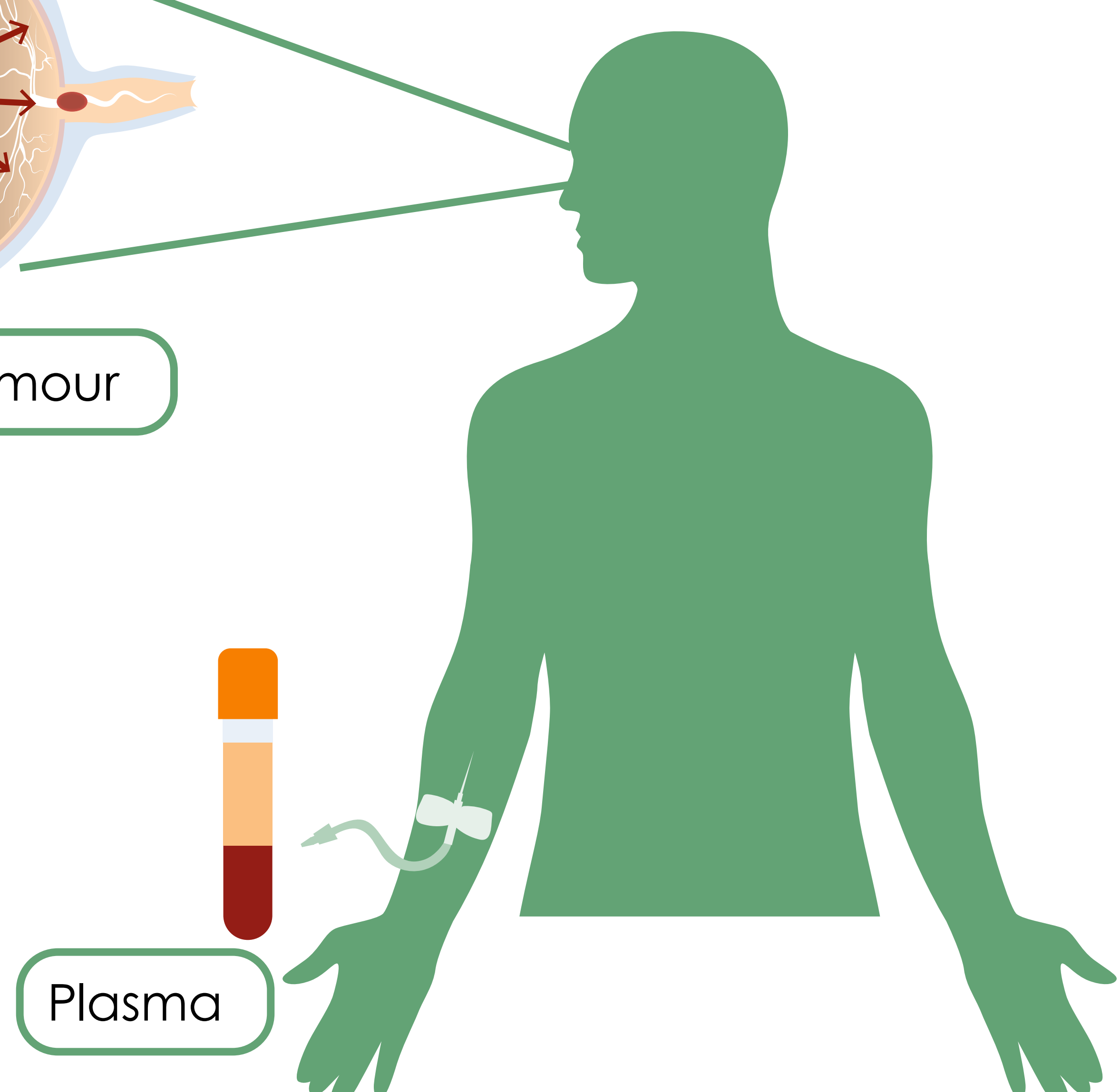
Hydroxyproline and methionine were significantly higher in the plasma of patients with POAG compared to controls



Aqueous humour

9 studies and **10 metabolites** included in the final meta-analysis

Alanine and methionine were consistently elevated in the aqueous humour and plasma, respectively, of patients with POAG



Based on this meta-analysis, alanine in aqueous humour and methionine in plasma are the most stable biomarkers for POAG

Study limitations and future outlook

Intrinsic biases in study selection

Changes found in the aqueous humour seem to be more consistent compared to plasma metabolite data, possibly due to the high sensitivity of metabolomics

Broader population and geographic locations in both healthy control subjects should be included in the future

POAG, primary open-angle glaucoma.

Reference
1. Tham Y-C, Li X, Wong TY, Quigley HA, Aung T, Cheng C-Y. Global Prevalence of Glaucoma and Projections of Glaucoma Burden through 2040. Ophthalmology. 2014;121(11):2081-2090.

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