Do findings on routine examination identify patients at risk for primary open-angle glaucoma? The Rational Clinical Examination systematic review

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CRD summary
This review concluded that increased cup-to-disc ratio, cup-to-disc ratio asymmetry, disc haemorrhage, and intraocular pressure were associated with an increased risk of primary open-angle glaucoma, but their absence did not rule it out. Despite the limitations of the review, the conclusions are likely to be reliable.

Authors' objectives
To assess the accuracy of routine examination to identify individuals at risk of primary open-angle glaucoma.

Searching
MEDLINE was searched for relevant English-language articles, from 1950 to January 2013; search terms were reported. Reference lists and citations of retrieved articles were manually searched.

Study selection
Studies assessing the accuracy of observable funduscopic findings (cup-to-disc ratio, cup-to-disc asymmetry, or disc haemorrhage) and intraocular pressure, in identifying patients at risk of primary open-angle glaucoma, were eligible for inclusion. Studies that recruited a few patients with other types of glaucoma were included in the review. Case reports were excluded. Demographic risk factors were assessed, but are not critiqued in this commentary.

In all the included studies, glaucoma was diagnosed by a single ophthalmologist or by consensus among a group of ophthalmologists. The gold standard used to assess the optic disc was either stereo disc photos (assessed by a trained observer) or slit-lamp biomicroscopy (assessed by an ophthalmologist). All studies included formal visual field eye examinations, and the gold standard to check intraocular pressure was Goldmann tonometry. The overall prevalence of primary open-angle glaucoma was 2.6%.

The authors did not state how many reviewers screened studies for inclusion.

Assessment of study quality
Studies were assessed according to the Rational Clinical Examination Series quality score. This rates studies for their use of a criterion standard, their sample size, and whether recruitment was consecutive. Only level one and two studies that recruited random samples were included in the review.

The authors did not state how many reviewers assessed the quality.

Data extraction
The data were extracted to calculate sensitivity, specificity, and positive and negative likelihood ratios, with 95% confidence intervals.

The authors did not state how many reviewers extracted the data.

Methods of synthesis
Where four or more studies were available, a bivariate random-effects model was used to produce summary positive and negative likelihood ratios. Where three studies were available, the data were combined using a univariate random-effects model.

Statistical heterogeneity was assessed using Cochran’s Q test and I². Analyses were conducted for different cut-off points for intraocular pressure. Where outcomes were reported in only two studies, or where studies counted eyes, rather than patients, a narrative synthesis was reported.

Results of the review
Thirty-four studies met the inclusion criteria, with over 86,000 participants (range 175 to 6,142).

**Cup-to-disc ratio:** In seven studies, the likelihood of primary open-angle glaucoma increased with increasing cup-to-disc ratio. Where the threshold was a ratio of 0.7 or more (five studies), the positive likelihood ratio was 14 (95% CI 5.3 to 39) and the negative likelihood ratio was 0.62 (95% CI 0.53 to 0.71).

**Ratio asymmetry:** In four studies, the likelihood of primary open-angle glaucoma increased with increasing asymmetry. A cut-off of at least 0.3 (three studies) gave a positive likelihood ratio of 7.3 (95% CI 3.3 to 16) and negative likelihood ratio of 0.89 (95% CI 0.83 to 0.94).

**Disc haemorrhage:** In five studies, the positive likelihood ratio for primary open-angle glaucoma was 12 (95% CI 2.9 to 48) and the negative likelihood ratio was 0.94 (95% CI 0.83 to 0.98).

**Intraocular pressure:** In 29 studies, as the intraocular pressure cut-off increased the positive likelihood ratio remained constant, but the negative likelihood ratio increased. A cut-off of 22mmHg or higher (19 studies) had a positive likelihood ratio of 13 (95% CI 8.2 to 17) and negative likelihood ratio of 0.65 (95% CI 0.55 to 0.76).

**Authors' conclusions**
Increased cup-to-disc ratio, ratio asymmetry, disc haemorrhage, and intraocular pressure were associated with an increased risk of primary open-angle glaucoma, but their absence did not rule it out.

**CRD commentary**
The review addressed a clear question, supported by reproducible inclusion criteria. The search was limited to one database and studies published in English, so relevant studies could have been missed. The authors did not report any methods to reduce error and bias in the review process. Appropriate criteria were used to assess study quality, but they did not cover all relevant biases. Inclusion was restricted to studies in the two highest quality categories. Appropriate methods of synthesis were used.

Despite the limitations of the review, the evaluation was based on a large number of patients, and the review's conclusions reflect the evidence presented. Therefore the conclusions are likely to be reliable.

**Implications of the review for practice and research**

**Practice:** The authors stated that the data supported examination by an ophthalmologist as the most accurate way to detect glaucoma. Intraocular pressure was the most important risk factor for primary open-angle glaucoma, but this was insufficient as a single diagnostic test because low pressure did not rule out glaucoma. They supported an age-based approach, as recommended by the American Academy of Ophthalmology, with frequent follow-up for patients with risk factors for glaucoma, at the clinician's discretion.

**Research:** The authors did not state any implications for research.

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