Title:

Glaucoma in UK Biobank: A Comparison of Diagnostic- Versus Treatment-based Definitions

Schierding W[1,2,*], Khoo A[2], Akeroyd E[1,2], Butterworth AS[3,4,5,6,7,], Danesh J[3,4,5,6,7,8], Danesh-Meyer HV[1,2]

[1] Department of Ophthalmology, University of Auckland, Auckland, New Zealand [2] Vision Research Foundation, Auckland, New Zealand [3] British Heart Foundation Cardiovascular Epidemiology Unit, Department of Public Health and Primary Care, University of Cambridge, Cambridge, UK. [4] Victor Phillip Dahdaleh Heart and Lung Research Institute, University of Cambridge, Cambridge, UK. [5] British Heart Foundation Centre of Research Excellence, School of Clinical Medicine, Addenbrooke's Hospital, University of Cambridge, Cambridge, UK. [6] Health Data Research UK, Wellcome Genome Campus and University of Cambridge, Hinxton, UK. [7] NIHR Blood and Transplant Research Unit in Donor Health and Behaviour, University of Cambridge, Cambridge, UK. [8] Department of Human Genetics, Wellcome Sanger Institute, Hinxton, UK.
* presenting author

Abstract:

PURPOSE

To compare, in the context of an observational cohort study of 503,325 participants in UK Biobank, associations of established risk factors and severity biomarkers with different glaucoma disease definitions.

METHODS

Participants without glaucoma (n=481,772) were compared to those with: (1) a diagnosis of glaucoma based on self-report, hospital inpatient, or primary care records (“diagnosis-only”; n=16,154); or (2) a diagnosis plus evidence of treatment with glaucoma-specific medication or surgery (“diagnosed-and-treated”; n=7,012), either at baseline or during follow-up. Odds ratios (ORs) for associations of established risk factors (corneal-compensated intraocular pressure [IOPcc], polygenic risk score [PRS]) and clinical biomarkers of disease severity (macular retinal nerve fiber layer [mRNFL], ganglion cell layer [mGCL]) with different glaucoma definitions.

RESULTS

For participants in the highest 5% of IOPcc compared with the remainder, ORs were 23.6 (95% CI: 21.3-26.2) in the diagnosed-treated group versus 11.4 (10.6-12.3; $p<1x10^{-10}$ for difference) in the diagnosed-only group. Corresponding ORs were: 8.0 (6.9-9.2) vs 4.7 (4.2-5.3; $p=2.32x10^{-7}$ for difference) for the thinnest 5% mRNFL; 7.1 (6.1-8.3) vs 4.2 (3.7-4.7; $p=2.53x10^{-7}$ for difference) for the thinnest 5% mGCL; and 8.4 (7.9-8.8) vs 5.6 (5.4-5.9; $p<1x10^{-10}$ for difference) for the highest 5% PRS. There were similar patterns for the other risk factors studied.

DISCUSSION

Definitions of glaucoma that combine both diagnostic and treatment evidence yielded substantially stronger associations with disease risk factors and biomarkers than definitions based on diagnostic evidence alone, probably reflecting more advanced disease phenotypes and suggesting implications for studies of glaucoma in population biobanks.