

# Meta-analysis of genome-wide association studies identifies novel loci that influence cupping and the glaucomatous process

Springelkamp H, Höhn R, Mishra A, Hysi PG, Khor CC, Loomis SJ, Bailey JN, Gibson J, Thorleifsson G, Janssen SF, Luo X, Ramdas WD, Vithana E, Nongpiur ME, Montgomery GW, Xu L, Mountain JE, Gharahkhani P, Lu Y, Amin N, Karssen LC, Sim KS, van Leeuwen EM, Iglesias AI, Verhoeven VJ, Hauser MA, Loon SC, Despriet DD, Nag A, Venturini C, Sanfilippo PG, Schillert A, Kang JH, Landers J, Jonasson F, Cree AJ, van Koolwijk LM, Rivadeneira F, Souzeau E, Jonsson V, Menon G; Blue Mountains Eye Study - GWAS group, Weinreb RN, de Jong PT, Oostra BA, Uitterlinden AG, Hofman A, Ennis S, Thorsteinsdottir U, Burdon KP; NEIGHBORHOOD Consortium; Wellcome Trust Case Control Consortium (WTCCC) , Spector TD, Mirshahi A, Saw SM, Vingerling JR, Teo YY, Haines JL, Wolfs RC, Lemij HG, Tai ES, Jansonius NM, Jonas JB, Cheng CY, Aung T, Viswanathan AC, Klaver CC, Craig JE, Macgregor S, Mackey DA, Lotery AJ, Stefansson K, Bergen AA, Young TL, Wiggs JL, Pfeiffer N, Wong TY, Pasquale LR, Hewitt AW, van Duijn CM, Hammond CJ.

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Glaucoma is characterized by irreversible optic nerve degeneration and is the most frequent cause of irreversible blindness worldwide. Here, the International Glaucoma Genetics Consortium conducts a meta-analysis of genome-wide association studies of vertical cup-disc ratio (VCDR) , an important disease-related optic nerve parameter. In 21,094 individuals of European ancestry and 6,784 individuals of Asian ancestry, we identify 10 new loci associated with variation in VCDR. In a separate risk-score analysis of five case-control studies, Caucasians in the highest quintile have a 2.5-fold increased risk of primary open-angle glaucoma as compared with those in the lowest quintile. This study has more than doubled the known loci associated with optic disc cupping and will allow greater understanding of mechanisms involved in this common blinding condition.

Nat Commun. 2014 Sep 22;5:4883. doi: 10.1038/ncomms5883

<http://www.ncbi.nlm.nih.gov/pubmed/25241763>