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### **Purpose**

The thinning of the Retinal Nerve Fiber Layer (RNFL) is a key risk factor in the development of glaucoma. Our study aimed to construct and validate a polygenic risk score (PRS) for RNFL thickness, using the UK Biobank (UKB) cohort, to assess its association with primary open-angle glaucoma (POAG) and to determine its efficacy in improving glaucoma prediction.

### **Methods**

We conducted this study using 367,724 European participants from the UKB. We carried out a genome-wide association of RNFL from a subset of 52,902 individuals who participated in the optical coherence tomography imaging and extracted RNFL-associated single nucleotide polymorphisms. This information was used to create a weighted RNFL PRS for the remaining 314,822 independent individuals. We employed logistic regression to explore the relationship between the RNFL PRS and POAG. To quantify the discriminatory ability of the PRS on POAG, we used the area under the receiver operating characteristic curve (AUC).

### **Results**

Our analysis revealed a significant association between the RNFL PRS and POAG ( $P = 8.9 \times 10^{-7}$ ), after adjusting for age, sex, and other relevant PRSs (POAG, intraocular pressure, and vertical cup-to-disc ratio). The inclusion of the RNFL PRS in the predictive model resulted in a 1.1% increase in AUC, thereby enhancing the model's discriminatory power for POAG. Notably, individuals in the lowest (thinnest) quintile of the RNFL PRS were 1.30 (95% CI: [1.14, 1.49],  $P = 1.5 \times 10^{-4}$ ) times more likely to have POAG compared to those in the highest quintile.

### **Conclusions**

We determined that RNFL PRS is significantly associated with POAG and improves its prediction.