Multi-Ancestry, Multi-Trait Polygenic Risk Scores for Myopia: Improved Accuracy and Clinical Potential

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Background: Myopia is a leading cause of visual impairment worldwide, with prevalence increasing dramatically due to societal changes such as reduced time spent outdoors. Despite these environmental influences, within populations myopia and its underlying quantitative trait, spherical equivalent refractive error (SERE), are both highly heritable. While optical correction can restore visual acuity, myopia confers markedly elevated risks of severe complications including retinal detachment.

Methods: We evaluated whether a polygenic risk score (PRS) could identify children at high genetic risk of myopia who might benefit from early preventive interventions. To improve on the limited accuracy of prior PRS, we assembled large-scale genome-wide association studies (GWAS) of SERE, myopia, hyperopia, and related ocular traits. Using a multi-trait framework that accounted for genetic correlations and sample overlap, we combined data from the UK Biobank, Million Veteran Program, FinnGen, and the Consortium for Refractive Error and Myopia, encompassing individuals of European, Asian, African, and Admixed American ancestry. PRS were derived using SBayesRC and validated in independent samples from UK Biobank and All of Us.

Results: The PRS explained 19% of SERE variance in individuals of European ancestry, outperforming previous models and alternative construction methods such as PRS-CSx. Prediction accuracy declined with increasing genetic distance from Europeans (R^2 = 13% in South Asians, 10% in East Asians, and 8% in Africans).

Conclusions: This new multi-trait PRS substantially improves prediction of refractive error, particularly in European populations. In clinical settings, it could guide proven early interventions, such as increased outdoor time, myopia-control contact lenses, or atropine drops, for children at greatest genetic risk. Genetically informed prevention represents a promising avenue to mitigate the growing global burden of myopia.