

https://dspace.org/

Performance of Polygenic Risk Scores for Primary OpenAngle Glaucoma in Populations of African Descent

Jennifer M Chang-Wolf; Tyler G Kinzy; Sjoerd J Driessen; Lauren A Cruz; Susan Williams ...

AMER MEDICAL ASSOC
https://hdl.handle.net/10539/48761
WOS

Downloaded from a DSpace repository. https://dspace.org/

JAMA Ophthalmology | Original Investigation

Performance of Polygenic Risk Scores for Primary Open-Angle Glaucoma in Populations of African Descent

Jennifer M. Chang-Wolf, MD; Tyler G. Kinzy, MS; Sjoerd J. Driessen, MD; Lauren A. Cruz, MPH; Sudha K. Iyengar, PhD; Neal S. Peachey, PhD; Tin Aung, MBBS, MMed, PhD; Chiea Chuen Khor, MD, PhD; Susan E. Williams, MD, PhD; Michele Ramsay, BSc, MSc, PhD; Olusola Olawoye, MBBS, MSc, PhD; Adeyinka Ashaye, MD; Caroline C. W. Klaver, MD, PhD; Michael A. Hauser, PhD; Alberta A. H. J. Thiadens, MD, PhD; Jessica N. Cooke Bailey, PhD, MA; Pieter W. M. Bonnemaijer, MD, PhD; for the Genetics in Glaucoma Patients of African Descent (GIGA) Study Group; for the Genetics of Glaucoma in People of African Descent (GGLAD) Study Group; for the Million Veteran Program (MVP)

IMPORTANCE Primary open-angle glaucoma (POAG) polygenic risk scores (PRSs) continue to be evaluated in primarily European-ancestry populations despite higher prevalence and worse outcomes in African-ancestry populations.

OBJECTIVE To evaluate how established POAG PRSs perform in African-ancestry samples from the Genetics in Glaucoma Patients of African Descent (GIGA), Genetics of Glaucoma in Individuals of African Descent (GGLAD), and Million Veteran Program (MVP) datasets and compare these with European-ancestry samples.

DESIGN, SETTING, AND PARTICIPANTS This was a multicenter, cross-sectional study of POAG cases and controls from Tanzania, South Africa, Nigeria, Ghana, and the US. Included were individuals of African descent from South Africa and Tanzania from the GIGA dataset; individuals of African descent from Ghana, Nigeria, and the US from the GGLAD dataset; and individuals of African or European descent from the US in the MVP dataset. Data were analyzed from January 2022 to July 2023.

EXPOSURES Three PRSs derived from large meta-analyses of European and Asian populations, namely Gharahkhani et al (Gharahkhani PRS), Han et al (Han PRS), and Craig et al (Craig PRS).

MAIN OUTCOMES AND MEASURES Odds ratios (ORs) for POAG risk stratification comparing the highest and lowest quintiles; area under the receiver operating characteristic curve (AUROC), and liability coefficient of determination (R^2) for the addition of PRS to a baseline of age, sex, and first 5 principal components.

RESULTS A total of 11 673 cases and 66 432 controls were included in this study across 7 ancestral groups. Mean (SD) age of the total participants was 76.9 (8.7) years, with 74 304 males (95.1%). The following were included in each dataset: GIGA (663 cases, 476 controls), GGLAD (1471 cases, 1482 controls), and MVP (9559 cases, 64 474 controls). Increases in ORs were found for the highest POAG risk quintile ranging from an OR of 1.68 (95% CI, 1.17-2.43) in Ghanaians to 7.05 (95% CI, 2.73-19.6) in the South African multiple ancestry group (which derives from at least 5 distinct ancestral groups: Khoisan, Bantus, Europeans, Indians, and Southeast Asians) with the Gharahkhani PRS. The Han PRS showed OR increases for the highest POAG risk quintile ranging from 2.27 (95% CI, 1.49-3.47) in African American individuals in the GGLAD dataset to 7.24 (95% CI, 6.47-8.12) in Europeans. The Craig PRS predicted OR increases in the highest quintile for all groups ranging from 1.51 (95% CI, 1.05-2.18) in Ghanaians to 6.31 (95% CI, 5.67-7.04) in Europeans. However, AUROC and R^2 increases above baseline were lower for all African-ancestry compared with European-ancestry groups in the 3 tested PRSs.

CONCLUSIONS AND RELEVANCE In this cross-sectional study, despite some improvements in OR-based risk stratification using the Gharahkhani PRSs, Han PRSs, and Craig PRSs, consistently lower improvements in AUROC and R^2 for African-ancestry compared with European-ancestry groups highlight the need for risk prediction models tailored to diverse populations.

JAMA Ophthalmol. 2025;143(1):7-14. doi:10.1001/jamaophthalmol.2024.4784
Published online November 14, 2024.

Invited Commentary page 9

Supplemental content

Author Affiliations: Author affiliations are listed at the end of this article.

Group Information: The members of the Genetics in Glaucoma Patients of African Descent (GIGA) Study Group, Genetics of Glaucoma in People of African Descent (GGLAD) Study Group, Million Veteran Program (MVP), and Cooperative Studies Program (CSP) appear in Supplement 2.

Corresponding Author: Pieter Bonnemaijer, MD, PhD, Department of Epidemiology, Erasmus Medical Center, NA2808, Dr. Molewaterplein 40, 3015 GD Rotterdam, the Netherlands (p.bonnemaijer@erasmusmc.nl).

© 2024 American Medical Association. All rights reserved, including those for text and data mining, AI training, and similar technologies.

Disproportionately affecting those of African ancestry, primary open-angle glaucoma (POAG) is a leading cause of irreversible blindness worldwide and is projected to become more prevalent in the coming decades.[1-3] POAG affected an estimated 76 million people globally in 2020 and is projected to affect nearly 120 million by 2040, making it a significant cause of irreversible blindness.[4-7] People of African descent face a higher risk, with up to 7 times the likelihood of developing POAG and experiencing blindness 4 times more frequently than those of European descent.[8,9] Risk stratification based on clinical and demographic data has long been used to aid patient care, which enables the identification of patients with high-risk POAG for more frequent follow-up or more aggressive clinical management.[10-13] Adding genetic data in the form of polygenic risk scores (PRSs) further improves risk stratification.[14]

Despite the disproportionate impact on individuals of African ancestry, genetic studies on POAG have focused on European and Asian populations, leaving a gap in understanding the genetic factors in African ancestral groups.[15-18] Recent genomic research advancements allow genetic data to enhance disease risk prediction. PRSs integrate variants from genome-wide association studies (GWAS) to predict disease risk. However, the construction of these PRSs currently relies heavily on data derived from European populations, raising concerns about their applicability and transferability to other populations with higher incidences of the target diseases.[16,19-22]

PRS approaches have performed well in POAG, predicting advanced glaucoma risk and influencing treatment decisions.[23-25] Importantly, these PRSs were constructed from and applied to population samples that were primarily European and Asian and are thus potentially more reflective of the genetic architecture of those groups. In this study, we evaluated the performance of these tools for their ability to stratify POAG risk in individuals of African ancestry from South Africa, Tanzania, Ghana, Nigeria, and the US.

Key Points

Question How do published polygenic risk scores (PRSs) for primary open-angle glaucoma (POAG) perform in African-ancestry compared with European-ancestry groups?

Findings In this cross-sectional study comparing 3 PRSs and including 11 673 cases and 66 432 controls across 7 ancestral groups, modest odds ratio increases were detected for the highest POAG risk quintile in Tanzanians, South Africans, Ghanaians, African Americans, and Europeans. However, overall predictive performance remains limited for African-ancestry compared with European-ancestry groups in terms of area under the curve and coefficient of determination.

Meaning Results suggest that despite some improvements in POAG risk stratification among African-ancestry groups, this study underscores the need for further research to develop more accurate risk prediction models tailored to diverse populations for equitable health care outcomes.

Methods

The Genetics in Glaucoma Patients of African Descent (GIGA) study, the Genetics of Glaucoma in People of African Descent (GGLAD) study, and the Million Veteran Program (MVP) adhered to the tenets of the Declaration of Helsinki, received ethical approval from the local institutional review boards, and obtained informed consent from all participants with no stipend or other incentive to participate. Only complete cases with age, sex, genotype, and phenotype data were included. This study followed the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) reporting guidelines.[26]

Study Population

GIGA is a multicenter POAG case-control study of individuals from the Groote Schuur Hospital (Cape Town, South Africa), Muhimbili National Hospital, and CCBRT Disability Hospital (Dar es Salaam, Tanzania).[27] The GIGA study included Tanzanians, Black South African people, and a group of individuals of multiple ancestries, which derives from at least 5 distinct ancestral groups: Khoisan, Bantus, Europeans, Indians, and Southeast Asians and for whom we use the term *South African multiple ancestry*.[28] Participants from the GGLAD discovery dataset included individuals of African descent recruited from Ghana (Lions International Eye Centre and Korle-Bu Teaching Hospital), Nigeria (University of Ibadan, University of Nigeria, and Nigerian Navy Reference Hospital), and North Carolina in the US (Duke University, Durham, North Carolina).[29-31] The MVP is a national research program sponsored by the Department of Veterans Affairs (VA) Office of Research and Development that includes health, genetic, and lifestyle information from 1 million US military Veterans who consented to participate in an observational cohort study and mega biobank. The genetic ancestry of over 450 000 MVP individuals with available genome-wide data was determined using the harmonized ancestry and race/ethnicity algorithm.[32,33]

Genotyped data from the GIGA and GGLAD study groups were imputed to 1000 Genomes (1000G) phase 3, version 5.[34] MVP samples were imputed on either the 1000G phase 3, version 5, reference panel or the African Genome Resource (not publicly available), which comprises all 1000G samples with an additional 2000 samples from Uganda and 100 samples from each of 5 populations in Ethiopia, Egypt, Namibia (Nama/Khoesan), and South Africa (Zulu).[32,35]

POAG Definition

GIGA POAG cases met International Society for Geographical and Epidemiological Ophthalmology classification categories 1 or 2, defined by a definite visual field defect and vertical cup disc ratio (VCDR) of greater than or equal to 0.7 or greater than 0.8 without visual field testing.[36] Cases had an open angle on gonioscopy and onset age older than 35 years. Controls underwent similar assessments and were characterized by no glaucoma signs or family history, intraocular pressure (IOP) less than or equal to 21 mm Hg, VCDR less than 0.5, VCDR intereye asymmetry less than 0.2, and age older than 55 years.[27,30,31,37] The GGLAD POAG definition included the presence of glaucomatous optic neuropathy characterized by loss

© 2024 American Medical Association. All rights reserved, including those for text and data mining, AI training, and similar technologies.

of neuroretinal rim, VCDR greater than 0.7, intereye asymmetry greater than 0.2, and glaucoma-associated notching. Control samples were recruited from hospitals or the general population, with hospital-based controls being older than 40 years, free from (family history of) glaucoma or major eye diseases, IOP less than 21 mm Hg, open angles, healthy optic nerves, and normal visual fields. MVP cases and controls were defined by a computable phenotyping algorithm based on *International Classification of Diseases-Clinical Modification* codes, *Current Procedural Terminology* codes, and prescriptions in the VA computerized patient record system.[38,39]

Statistical Analysis

We tested 3 PRSs using weighted additive models where the imputed dosage of each risk allele (*j*) was multiplied by its calculated β (log odds ratio [OR]) and summed using PLINK2 to produce a score for each individual *(i)*[40]:

$$\text{score}_i = \Sigma^{k}_{j=1} \beta_j M_{ij}$$

1. Gharahkhani PRS (k = 111): Based on 127 POAG-associated variants identified in the largest to date cross-ancestry single-trait POAG GWAS meta-analysis.[41] To reduce potential bias due to inclusion of overlapping African ancestral data from the GIGA and GGLAD studies, we applied a fixed-effects inverse variance-weighted meta-analysis to 239 168 controls and 23 612 POAG cases of European or Asian descent. Without the African datasets, 115 single-nucleotide variants (SNVs) maintained genome-wide significance. The X chromosome was excluded because it was unavailable in some cohorts, leaving 111 autosomal SNVs.
2. Given potential differences in linkage disequilibrium (LD) patterns, we developed a modified LD proxy PRS (k = 111) to incorporate SNV proxies while accounting for between-population LD variation. We analyzed SNV transferability via the local approach and evaluated a 500-kb window around each variant for SNVs with LD r^2 greater than 0.2 (as defined by the 1000 Genomes African subset).[27] We examined these for evidence of higher association in the African-only GWAS.[41] Of these, 63 were nominally associated (P < .05), and the lead SNV was replaced with the local replacement SNV.
3. Han PRS (k = 223): Based on multitrait GWAS meta-analysis of POAG, VCDR, and IOP that identified 263 novel POAG loci, of which we included 223 SNVs from the European discovery set that replicated in an independent 23andMe cohort in which the P value remained <.001 after Bonferroni correction to avoid inflation due to overlap between Asian and African samples.[23]
4. Craig PRS (k = 2673): Based on a POAG PRS derived from 67 040 UK Biobank samples by combining multiple endophenotypes (eg, VCDR and IOP) in multivariate analysis and validating the 2673 SNVs with $P \leq .001$ in independent European datasets.[25]

To investigate score value distributions across study groups, we plotted PRS densities standardized with a mean of 0 and an SD of 1 (eFigure 1 in Supplement 1). To account for potential nonlinear association and facilitate comparisons between different sample sizes, we constructed PRS quintiles. To adjust for confounding factors, we included age, sex, and the first 5 principal components (PCs) as covariates. For each quintile, we used a logistic regression model to estimate ORs of POAG risk and 95% CIs.

Aside from quintile stratification, we implemented logistic regression models of baseline alone (ie, age, sex, and 5 PCs) and with the addition of continuous PRS values. We examined the area under the receiver operating characteristic curve (AUROC) and used the DeLong test to compare area under the curve increases from the addition of PRS with the baseline models. We additionally evaluated the added value of continuous PRSs to baseline by determining increases in R^2 coefficients of determination. We computed R^2 on the liability scale to account for varying proportions of phenotypic variance explained by each PRS.[42,43] Case/control ratios in this study ranged from 0.09 in the European American group to 0.70 in the South African Black group. We fixed disease prevalence at 2.4% for comparison, although prevalence may vary across ancestral groups.[44] Data were analyzed from January 2022 to July 2023, using R statistical software, version 4.2.1 (R Foundation for Statistical Computing).

Results

Study Demographics for POAG Cases and Controls

A total of 11 673 cases and 66 432 controls were included in this study across 7 ancestral groups: Tanzanian (366 cases, 329 controls), South African multiple ancestry (179 cases, 96 controls), South African Black (118 cases, 51 controls), Nigerian (125 cases, 185 controls), Ghanaian (640 cases, 690 controls), African American (4627 cases, 6272 controls), and European American (5618 cases, 58 809 controls). The African American group comprised 2 subgroups: the GGLAD dataset (706 cases, 607 controls) and MVP dataset (3921 cases, 5665 controls). The following were included in each dataset: GIGA (663 cases, 476 controls), GGLAD (1471 cases, 1482 controls), and MVP (9559 cases, 64474 controls). Mean (SD) age of the total participants was 76.9 (8.7) years, with 3801 females (4.9%) and 74 304 males (95.1%). Study sample characteristics are presented in the **Table**. Sex proportions differed between cases and controls in the Tanzanian (female sex: 125 of 366 cases [34.2%], 172 of 329 controls [52.3%]; $P = 2.1 \times 10^{-6}$), South African Black (female sex: 62 of 118 cases [52.5%], 40 of 51 controls [78.4%]; $P = 2.8 \times 10^{-3}$), Nigerian (female sex: 48 of 125 cases [38.4%], 104 of 185 controls [56.2%]; $P = 3.1 \times 10^{-3}$), African American MVP (female sex: 216 of 3921 cases [5.5%], 171 of 5665 controls [3.0%]; $P = 1.9 \times 10^{-9}$), and European American (female sex: 211 of 5618 cases [8.7%], 1314 of 58 809 controls [2.2%]; $P = 5.91 \times 10^{-13}$) groups based on χ^2 testing. The mean (SD) age differed between cases and controls in the South African Black (62.9 [10.7] years; $P = 2 \times 10^{-4}$), Tanzanian (64.8 [9.8] years; $P = 3.4 \times 10^{-6}$), Ghanaian (59.6 [11.1] years; $P = 4.5 \times 10^{-23}$), and African American GGLAD (61.3 [12.7] years; $P = 8.1 \times 10^{-94}$) as well as African American MVP (74.2 [7.9] years; $P = 2.2 \times 10^{-16}$) groups based on Welch t test.

© 2024 American Medical Association. All rights reserved, including those for text and data mining, AI training, and similar technologies.

Table. Demographic Summary[a]

Variable	GIGA			GGLAD			MVP	
	Tanzanian	South African multiple ancestry[b]	South African Black	Nigerian	Ghanaian	African American	African American	European American
No. (%)								
Total	695	275	169	310	1330	1313	9586	64 427
Cases	366 (52.7)	179 (65.1)	118 (69.8)	125 (40.3)	640 (48.1)	706 (53.8)	3921 (40.9)	5618 (8.7)
Controls	329 (47.3)	96 (34.9)	51 (30.2)	185 (59.7)	690 (51.9)	607 (46.2)	5665 (59.1)	58 809 (91.3)
Female sex, No. (%)								
Cases	125 (34.2)	93 (52.0)	62 (52.5)	48 (38.4)	279 (43.6)	336 (47.6)	216 (5.5)	211 (3.8)
Controls	172 (52.3)	54 (56.3)	40 (78.4)	104 (56.2)	297 (43.0)	279 (46.0)	171 (3.0)	1314 (2.2)
Male sex, No. (%)								
Cases	241 (65.8)	86 (48.0)	56 (47.5)	77 (61.6)	361 (56.4)	370 (52.4)	3705 (94.5)	5407 (96.2)
Controls	157 (47.7)	42 (43.8)	11 (21.6)	81 (43.8)	393 (56.9)	328 (54.0)	5494 (97.0)	57 495 (97.8)
P value (χ^2 test)	2.1×10^{-6}	.58	2.8×10^{-3}	3.1×10^{-3}	.88	.54	1.9×10^{-9}	5.91×10^{-13}
Age, mean (SD), y								
Total	64.8 (9.8)	69.7 (10.0)	62.9 (10.7)	63.5 (11.5)	59.6 (11.1)	61.3 (12.7)	74.2 (7.9)	78.2 (7.6)
Cases	63.2 (11.0)	70.5 (11.0)	61.3 (11.5)	63.7 (11.5)	62.7 (12.4)	67.4 (12.3)	71.2 (9.5)	78.2 (7.6)
Controls	66.6 (8.1)	68.3 (7.7)	66.8 (7.2)	63.4 (11.5)	56.7 (9.0)	54.2 (9.0)	76.2 (6.7)	78.2 (7.4)
P value (Welch *t* test)	3.4×10^{-6}	.06	2×10^{-4}	.82	4.5×10^{-23}	8.1×10^{-94}	2.2×10^{-16}	.47

Abbreviations: GGLAD, Genetics of Glaucoma in Individuals of African Descent; GIGA, Genetics in Glaucoma Patients of African Descent; MVP, Million Veteran Program.

[a] The table presents information for the included population groups across different demographic variables.

[b] The South African multiple ancestry group derives from at least 5 distinct ancestral groups: Khoisan, Bantus, Europeans, Indians, and Southeast Asians.

POAG Risk Stratification by PRS

We evaluated the performance of the 3 PRS in 8 study groups by comparing ORs categorized into quintiles, as illustrated in **Figure 1** and detailed in eTable 1 in Supplement 1. The distribution of case proportions by quintile is visually depicted in eFigure 2 in Supplement 1. **Figure 2** shows the increase in AUROC compared with the baseline model; detailed AUROC values are provided in eTable 2 in Supplement 1. Additionally, we examined R^2 values on the liability scale to further characterize the predictive accuracy of the evaluated scores (eTable 3 in Supplement 1). Here, we present the results of these measures separately for each score.

Gharahkhani PRS

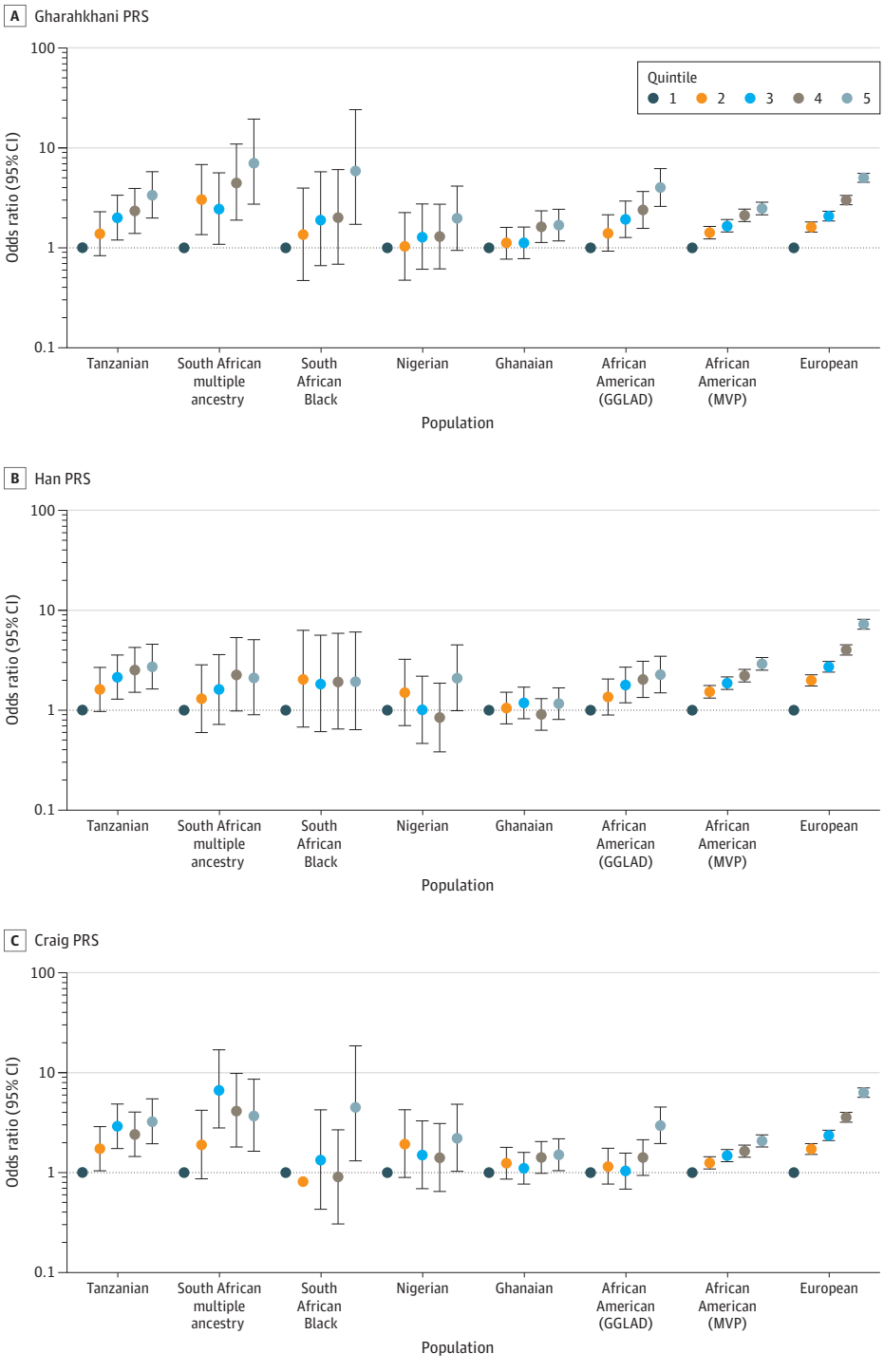
Using the Gharahkhani PRS consisting of 111 SNVs, we observed an increase in the OR for POAG risk within the highest PRS quintile, compared with the lowest quintile across all groups except Nigerian (Figure 1). Relative to the European American group in this study (OR, 5.02; 95% CI, 4.54-5.57), the ORs within the highest quintile were increased but had wider CIs in the South African groups. Specifically, increases in ORs were found for the highest POAG risk quintile ranging from an OR of 1.68 (95% CI, 1.17-2.43) in Ghanaians to 7.05 (95% CI, 2.73-19.6) in the South African multiple ancestry group with the Gharahkhani PRS. The OR was 5.89 (95% CI, 1.72-24.30) for the highest quintile of the South African Black group compared with the lowest quintile and 7.05 (95% CI, 2.73-19.60) in the South African multiple ancestry group (Figure 1 and eTable 1 in Supplement 1). The performance of the GRS compared with a baseline model of age, sex, and the first 5 PCs was assessed by the AUROC. We observed a gain in the AUROC for the Tanzanian, South African multiple ancestry, African American (GGLAD and MVP), and European American groups (Figure 2 and eTable 2 in Supplement 1). However, the increase in AUROC was relatively modest in the Tanzanian (0.03 AUROC improvement from 0.66 baseline, $P = .03$) and African American (GGLAD: 0.02 AUROC improvement from 0.81 baseline, $P < .001$; MVP: 0.01 AUROC improvement from 0.69 baseline, $P < .001$) groups compared with the European American (0.06 AUROC improvement from 0.52 baseline, $P < .001$) group (eTable 2 in Supplement 1). We also evaluated the estimated proportion of POAG variance explained by the score. When comparing the genetic prediction performance of the Gharahkhani PRS from the African ancestral groups with the European American group, we observed lower phenotypic variance explained across all the African groups. Adding PRS to the baseline model, an improvement of the liability-R^2 value was only detected in the South African multiple ancestry group (0.03 R^2 increment over 0.01 baseline) and European American group (0.06 R^2 increment over 0.002 baseline) (eTable 3 in Supplement 1). We attempted to consider differences in LD using the LD proxy score, however, this approach yielded unremarkable results across all groups when compared with the original Gharahkhani PRS (eTable 4 in Supplement 1).

Han PRS

The Han PRS, consisting of 223 SNVs, showed increases in ORs for the highest genetic risk quintile compared with the lowest risk quintile in the Tanzanian, Ghanaian, GGLAD and MVP African American, and European American groups (Figure 1 and eTable 1 in Supplement 1). In the European American group, the Han PRS demonstrated the most substantial OR estimate for the highest quintile compared with the lowest among all tested scores (7.24; 95% CI, 6.47-8.12, $P < .001$) (eTable 1 in Supplement 1). In contrast, when comparing the highest with the lowest quintiles, the OR estimates were lower in the Han PRS than in the Gharahkhani PRS in the Tanzanian, South African, Ghanaian, and GGLAD African American groups. Consequently, the Han PRS only exhibited superior high-risk identification in the MVP African American and

© 2024 American Medical Association. All rights reserved, including those for text and data mining, AI training, and similar technologies.

Figure 1. Odds Ratios by Quintile

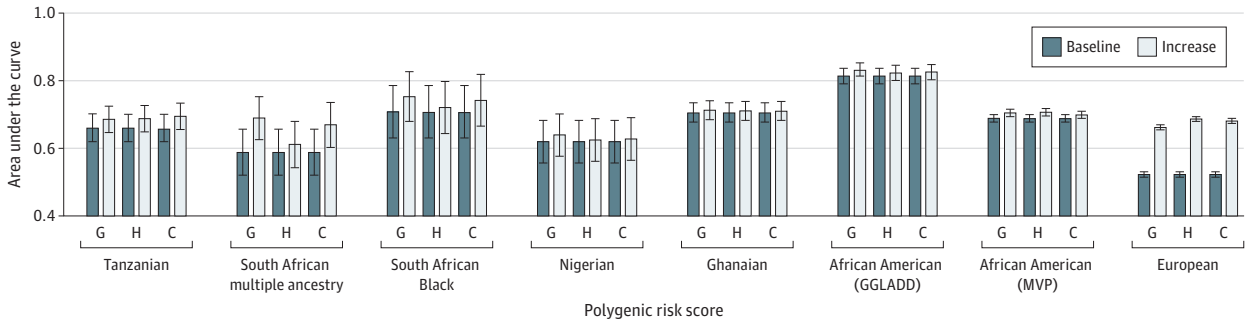


The odds ratios (log scale) of risk for primary open-angle glaucoma from logistic regression by quintile for each of 8 study groups are displayed using 3 polygenic risk score (PRS) types: Gharahkhani PRS (A), Han PRS (B), and Craig PRS (C). Odds ratios (on a log scale) and 95% CIs are presented, allowing for comparison of risk across quintiles within each risk score type. GGLAD indicates Genetics of Glaucoma in People of African Descent; MVP, Million Veteran Program.

European American groups. The prediction performance of the Han PRS demonstrated an improvement in the AUROC compared with the baseline model in the Tanzanian (0.03 AUROC improvement from 0.66 baseline, $P = .02$), African American (GGLAD: 0.01 AUROC improvement from 0.82 baseline, $P = .005$; MVP: 0.02 AUROC improvement from 0.71 baseline, $P < .001$), and European American (0.16 AUROC improvement from 0.52 baseline, $P < .001$) groups (the H blue bars) (Figure 2 and eTable 2 in Supplement 1). Regarding R^2 by the Han PRS, increases for African ancestry groups were modest relative to the European American group. We only observed an improvement exceeding the contribution of the baseline alone in the European American group (0.08 R^2 increment over 0.002 baseline) (eTable 3 in Supplement 1). The Han PRS outperformed all other scores regarding AUROC and R^2

© 2024 American Medical Association. All rights reserved, including those for text and data mining, AI training, and similar technologies.

Figure 2. Improvement in Area Under the Receiver Operating Characteristic (AUROC) Curve Adding a Polygenic Risk Score (PRS) to the Baseline Model by Population and PRS



The improvement of the AUROC of a model with the genetic risk score/PRS compared with a baseline model of sex, age, and 5 principal components is shown. The data are organized by population groups, including Tanzanian, South African multiple ancestry (which derives from at least 5 distinct ancestral groups: Khoisan, Bantus, Europeans, Indians, and Southeast Asians), South African Black, Nigerian, Ghanaian, African American (Genetics of Glaucoma in People of African Descent [GGLAD]), African American (Million Veteran Program [MVP]), and European. The heights of the bars reflect the AUROC increase values, and each bar is color-coded according to baseline vs values after addition of the Gharahkhani PRS (designated G), Han PRS (designated H), and Craig PRS (designated C) as indicated on the x-axis.

increases within the MVP African American and European American groups.

Craig PRS

Of the 3 scores, only the Craig PRS produced OR increases for the highest quintile in all tested groups ranging from 1.51 (95% CI, 1.05-2.18) in Ghanaians to 6.31 (95% CI, 5.67-7.04) in Europeans (Figure 1 and eTable 1 in Supplement 1). Prediction of POAG risk using the Craig PRS score increased the AUROC in the same groups as the Gharahkhani PRS (the G blue bars): Tanzanian (0.04 AUROC improvement from 0.66 baseline, $P = .007$), South African multiple ancestry (0.08 AUROC improvement from 0.59 baseline, $P = .03$), African American (GGLAD: 0.01 AUROC improvement from 0.81 baseline, $P = .002$; MVP: 0.01 AUROC improvement from 0.69 baseline, $P < .001$), and European American (0.16 AUROC improvement from 0.52 baseline, $P < .001$) (Figure 2 and eTable 2 in Supplement 1). Increases in R^2 were smaller for all African groups than for European Americans. The Craig PRS showed a slight improvement in R^2 for the South African multiple ancestry group compared with the baseline (0.03 R^2 increment over 0.01 baseline) (eTable 3 in Supplement 1). Conversely, the increase in R^2 within the European American group was more considerable (0.07 R^2 increment over 0.002 baseline) (eTable 3 in Supplement 1), mirroring the performance observed with the Han PRS.

Discussion

This study evaluates 3 PRSs for POAG, derived from a meta-analysis of European and Asian population GWAS data, for distinguishing between cases and controls in a European ancestry group and 7 African ancestry groups. All 3 PRSs performed best for classifying POAG cases in the European American group, emphasizing the importance of constructing genetic risk scores using reference data from the same ancestral population as the study group. The improvement in AUROC remained modest for most African ancestral groups whereas performance was best in those groups with the highest proportion of European ancestry, the African American and South African multiple ancestry groups (Figure 2). Performance of risk scores is limited to stratifying individuals into case and control groups when comparing the lowest to the highest quintiles of genetic risk as defined by each risk score. This distinction does little to help guide clinical management.[45,46]

Strengths and Limitations

Our study has several strengths. We leverage ancestrally diverse data from 2 of the largest currently available datasets containing the genetic information of native African populations for glaucoma. However, even within African groups with low P values and relatively small CIs suggesting adequate power to detect differences, the OR gain was substantially higher in European groups. This suggests that the marked increase in ORs across quintiles of PRS in Europeans may not be solely attributable to higher statistical power but may also be influenced by ancestry-related factors. Others have reported this disparity in other diseases, and it has been suggested that this performance could be improved using models with more genetic variants.[15,21,47,48] Our data do not support this—the Gharahkhani PRS performed as well as or better than the 2 larger models. The most important contributing factor to poor overall performance is the lack of population-specific genetic risk data for glaucoma. It is well recognized that individuals of African ancestry are underrepresented in GWAS studies, resulting in a small number of associated genetic variants with potentially imprecise estimates of effect sizes.[49,50] At the same time, African continental and diaspora populations worldwide have very high levels of POAG.[51] Extensive GWAS studies that include diverse African ancestry populations hold great promise for advancing our understanding of POAG risk in African individuals to enhance clinical management of this understudied and underserved patient population.[52]

We also recognize several limitations in this study. Despite using 2 of the most extensive available datasets, our African datasets had low statistical power, especially the South African group.

© 2024 American Medical Association. All rights reserved, including those for text and data mining, AI training, and similar technologies.

This potentially limits the generalizability of our findings and emphasizes the need to support the implementation of more diverse genetic studies that include African populations. Furthermore, the GIGA and GGLAD studies draw cases and controls from hospital settings, whereas the MVP draws cases and controls from a defined cohort of VA medical center users. This difference in sampling methodology may impact the genetic risk profiles and the demographic composition, potentially accounting for the disparities observed in the baseline AUROC statistics. Moreover, the POAG definition in the MVP populations differed from that in the GIGA and GGLAD studies.

Conclusions

In this cross-sectional study, results suggest that adding genetic variants to the risk model moderately improved PRS performance for Africans, whereas more substantial improvements were seen in risk identification for Europeans. This emphasizes that simply including more variants in the PRS does not address the model performance disparity across ancestral populations and may reinforce it. Genetically diverse discovery datasets are necessary for building population-specific PRSs.

ARTICLE INFORMATION

Accepted for Publication: August 18, 2024.

Published Online: November 14, 2024. doi:10.1001/jamaophthalmol.2024.4784

Author Affiliations: Department of Epidemiology, Erasmus Medical Center, Rotterdam, the Netherlands (Chang-Wolf, Driessen, Klaver, Thiadens, Bonnemaijer); Department of Ophthalmology, Duke University, Durham, North Carolina (Chang-Wolf, Hauser); Department of Medicine, Duke University Medical Center, Durham, North Carolina (Chang-Wolf, Hauser); Cleveland Institute for Computational Biology, Case Western Reserve University, Cleveland, Ohio (Kinzy, Cruz, Iyengar, Cooke Bailey); Department of Population & Quantitative Health Sciences, Case Western Reserve University, Cleveland, Ohio (Kinzy, Cruz, Iyengar, Cooke Bailey); Research Service, VA Northeast Ohio Healthcare System, Cleveland, Ohio (Kinzy, Iyengar, Peachey, Cooke Bailey); Department of Pharmacology & Toxicology, Brody School of Medicine, East Carolina University, Greenville, North Carolina (Kinzy, Cooke Bailey); Center for Health Disparities, Brody School of Medicine, East Carolina University, Greenville, North Carolina (Kinzy, Cooke Bailey); Department of Ophthalmology, Erasmus Medical Center, Rotterdam, the Netherlands (Driessen, Klaver, Thiadens, Bonnemaijer); Cole Eye Institute, Cleveland Clinic Foundation, Cleveland, Ohio (Peachey); Department of Ophthalmology, Cleveland Clinic Lerner College of Medicine of Case Western Reserve University, Cleveland, Ohio (Peachey); Singapore Eye Research Institute, Singapore (Aung, Hauser); Genome Institute of Singapore, Agency for Science, Technology and Research, Singapore (Khor); Division of Ophthalmology, Department of Neurosciences, University of the Witwatersrand, Johannesburg, South Africa (Williams); Sydney Brenner Institute for Molecular Bioscience, Faculty of Health Sciences, University of the Witwatersrand, Johannesburg, South Africa (Ramsay); Department of Ophthalmology, College of Medicine, University of Ibadan, Ibadan, Nigeria (Olawoye, Ashaye); Department of Ophthalmology, Radboud University Medical Centre, Nijmegen, Gelderland, the Netherlands (Klaver); Institute of Molecular and Clinical Ophthalmology, Basel, Switzerland (Klaver); The Rotterdam Eye Hospital, Rotterdam, the Netherlands (Bonnemaijer).

Author Contributions: Drs Bonnemaijer and Cooke Bailey had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. Dr Chang-Wolf and Mr Kinzy are considered co-first authors of this work. Drs Cooke Bailey and Bonnemaijer are considered co-senior authors of this work.
Concept and design: Chang-Wolf, Kinzy, Driessen, Aung, Olawoye, Klaver, Thiadens, Cooke Bailey, Bonnemaijer.
Acquisition, analysis, or interpretation of data: Chang-Wolf, Kinzy, Driessen, Cruz, Iyengar, Peachey, Aung, Khor, Williams, Ramsay, Ashaye, Klaver, Hauser, Thiadens, Cooke Bailey, Bonnemaijer.
Drafting of the manuscript: Chang-Wolf, Kinzy, Aung, Thiadens, Cooke Bailey, Bonnemaijer.
Critical review of the manuscript for important intellectual content: All authors.
Statistical analysis: Chang-Wolf, Kinzy, Driessen, Khor, Ashaye, Thiadens, Bonnemaijer.
Obtained funding: Iyengar, Peachey, Olawoye, Klaver, Thiadens, Cooke Bailey, Bonnemaijer.
Administrative, technical, or material support: Chang-Wolf, Kinzy, Iyengar, Peachey, Aung, Olawoye, Hauser, Thiadens.
Supervision: Driessen, Klaver, Hauser, Thiadens, Cooke Bailey, Bonnemaijer.

Conflict of Interest Disclosures: Mr Kinzy reported receiving grants from National Institutes of Health and the Department of Veterans Affairs during the conduct of the study. Ms Cruz reported receiving grants from the National Institutes of Health during the conduct of the study. Dr Olawoye reported receiving grants from National Institute of Health H3 Africa during the conduct of the study. Dr Cooke Bailey reported receiving grants from National Institutes of Health and from Department of Veterans Affairs during the conduct of the study. Dr Bonnemaijer reported receiving grants from Brightfocus, Uitzicht, and Rottersamse Blindenbelangen during the conduct of the study. No other disclosures were reported.

Funding/Support: This study was supported in part by the BrightFocus Foundation, the Combined Ophthalmic Research Rotterdam Foundation, the Rotterdamse Stichting Blindenbelangen, the Landelijke Stichting voor Blinden en Slechtzienden, the Stichting Beheer Het Schild, Algemene Nederlandse Vereniging ter Voorkoming van Blindheid, and het Glaucoomfonds through Uitzicht; grant R01EY033829 from the National Institutes of Health (Dr Cooke Bailey, Mr Kinzy, and Dr Hauser); and data from the Million Veteran Program (MVP) were supported by the MVP Office of Research and Development, Veterans Health Administration, and by award I01 BX004557 (Dr Cooke Bailey, Mr Kinzy, Dr Iyengar, and Dr Peachey). Ms Cruz was supported by National Institutes of Health grants T32 HL007567 and T32 EY007157.

Role of the Funder/Sponsor: The funders had no role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; preparation, review, or approval of the manuscript; and decision to submit the manuscript for publication.

Group Information: The members of the Genetics in Glaucoma Patients of African Descent (GIGA) Study Group, Genetics of Glaucoma in People of African Descent (GGLAD) Study Group, Million Veteran Program (MVP), and Cooperative Studies Program (CSP) appear in Supplement 2.

Disclaimer: This publication does not represent the views of the Department of Veteran Affairs or the US government.

Data Sharing Statement: See Supplement 3.

REFERENCES

1. Quigley HA, Broman AT. The number of people with glaucoma worldwide in 2010 and 2020. *Br J Ophthalmol*. 2006;90(3):262-267. doi:10.1136/bjo.2005.081224

2. Jonas JB, Aung T, Bourne RR, Bron AM, Ritch R, Panda-Jonas S. Glaucoma. *Lancet*. 2017;390(10108):2183-2193. doi:10.1016/S0140-6736(17)31469-1

3. Varma R, Vajaranant TS, Burkemper B, et al. Visual impairment and blindness in adults in the US: demographic and geographic variations from 2015 to 2050. *JAMA Ophthalmol*. 2016;134(7):802-809. doi:10.1001/jamaophthalmol.2016.1284

4. Hattenhauer MG, Johnson DH, Ing HH, et al. The probability of blindness from open-angle glaucoma. *Ophthalmology*. 1998;105(11):2099-2104. doi:10.1016/S0161-6420(98)91133-2

5. Kwon YH, Fingert JH, Kuehn MH, Alward WLM. Primary open-angle glaucoma. *N Engl J Med*. 2009;360(11):1113-1124. doi:10.1056/NEJMra0804630

6. Allison K, Patel D, Alabi O. Epidemiology of glaucoma: the past, present, and predictions for the future. *Cureus*. 2020;12(11):e11686. doi:10.7759/cureus.11686

7. Tham YC, Li X, Wong TY, Quigley HA, Aung T, Cheng CY. Global prevalence of glaucoma and projections of glaucoma burden through 2040: a systematic review and meta-analysis. *Ophthalmology*. 2014;121(11):2081-2090. doi:10.1016/j.ophtha.2014.05.013

8. Bonnemaijer PWM, Lo Faro V, Sanyiwa AJ, et al; GIGA study group. Differences in clinical presentation of primary open-angle glaucoma between African and European populations. *Acta Ophthalmol*. 2021;99(7):e1118-e1126. doi:10.1111/aos.14772

9. Kyari F, Abdull MM, Bastawrous A, Gilbert CE, Faal H. Epidemiology of glaucoma in Sub-Saharan Africa: prevalence, incidence and risk factors.

© 2024 American Medical Association. All rights reserved, including those for text and data mining, AI training, and similar technologies.

Middle East Afr J Ophthalmol. 2013;20(2):111-125. doi:10.4103/0974-9233.110605

10. Weinreb RN, Aung T, Medeiros FA. The pathophysiology and treatment of glaucoma: a review. *JAMA*. 2014;311(18):1901-1911. doi:10.1001/jama.2014.3192

11. Gordon MO, Beiser JA, Brandt JD, et al. The Ocular Hypertension Treatment Study: baseline factors that predict the onset of primary open-angle glaucoma. *Arch Ophthalmol*. 2002;120(6):714-720. doi:10.1001/archopht.120.6.714

12. Chauhan BC, Mikelberg FS, Balaszi AG, LeBlanc RP, Lesk MR, Trope GE; Canadian Glaucoma Study Group. Canadian Glaucoma Study: 2. risk factors for the progression of open-angle glaucoma. *Arch Ophthalmol*. 2008;126(8):1030-1036. doi:10.1001/archopht.126.8.1030

13. Leske MC, Heijl A, Hyman L, Bengtsson B. Early Manifest Glaucoma Trial: design and baseline data. *Ophthalmology*. 1999;106(11):2144-2153. doi:10.1016/S0161-6420(99)90497-9

14. Wiggs JL, Pasquale LR. Genetics of glaucoma. *Hum Mol Genet*. 2017;26(R1):R21-R27. doi:10.1093/hmg/ddx184

15. Cooke Bailey JN, Funk KL, Cruz LA, et al. Diversity in polygenic risk of primary open-angle glaucoma. *Genes (Basel)*. 2022;14(1):111. doi:10.3390/genes14010111

16. Duncan L, Shen H, Gelaye B, et al. Analysis of polygenic risk score usage and performance in diverse human populations. *Nat Commun*. 2019;10(1):3328. doi:10.1038/s41467-019-11112-0

17. Fatumo S, Sathan D, Samtal C, et al. Polygenic risk scores for disease risk prediction in Africa: current challenges and future directions. *Genome Med*. 2023;15(1):87. doi:10.1186/s13073-023-01245-9

18. Fritsche LG, Ma Y, Zhang D, et al. On cross-ancestry cancer polygenic risk scores. *PLoS Genet*. 2021;17(9):e1009670. doi:10.1371/journal.pgen.1009670

19. Martin AR, Kanai M, Kamatani Y, Okada Y, Neale BM, Daly MJ. Clinical use of current polygenic risk scores may exacerbate health disparities. *Nat Genet*. 2019;51(4):584-591. doi:10.1038/s41588-019-0379-x

20. Majara L, Kalungi A, Koen N, et al. Low and differential polygenic score generalizability among African populations due largely to genetic diversity. *HGG Adv*. 2023;4(2):100184. doi:10.1016/j.xhgg.2023.100184

21. Kamiza AB, Toure SM, Vujkovic M, et al. Transferability of genetic risk scores in African populations. *Nat Med*. 2022;28(6):1163-1166. doi:10.1038/s41591-022-01835-x

22. Liu C, Zeinomar N, Chung WK, et al. Generalizability of polygenic risk scores for breast cancer among women with European, African, and Latinx Ancestry. *JAMA Netw Open*. 2021;4(8):e2119084. doi:10.1001/jamanetworkopen.2021.19084

23. Han X, Gharahkhani P, Hamel AR, et al; 23andMe Research Team; International Glaucoma Genetics Consortium. Large-scale multitrait genome-wide association analyses identify hundreds of glaucoma risk loci. *Nat Genet*. 2023;55(7):1116-1125. doi:10.1038/s41588-023-01428-5

24. Marshall HN, Mullany S, Han X, et al. High polygenic risk is associated with earlier initiation and escalation of treatment in early primary open-angle glaucoma. *Ophthalmology*. 2023;130(8):830-836. doi:10.1016/j.ophtha.2023.03.028

25. Craig JE, Han X, Qassim A, et al; NEIGHBORHOOD consortium; UK Biobank Eye and Vision Consortium. Multitrait analysis of glaucoma identifies new risk loci and enables polygenic prediction of disease susceptibility and progression. *Nat Genet*. 2020;52(2):160-166. doi:10.1038/s41588-019-0556-y

26. von Elm E, Altman DG, Egger M, Pocock SJ, Gøtzsche PC, Vandenbroucke JP; STROBE Initiative. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies. *J Clin Epidemiol*. 2008;61(4):344-349. doi:10.1016/j.jclinepi.2007.11.008

27. Bonnemaijer PWM, Iglesias AI, Nadkarni GN, et al; GIGA Study Group; Eyes of Africa Genetics Consortium; NEIGHBORHOOD Consortium. Genome-wide association study of primary open-angle glaucoma in continental and admixed African populations. *Hum Genet*. 2018;137(10):847-862. doi:10.1007/s00439-018-1943-7

28. Patterson N, Petersen DC, van der Ross RE, et al. Genetic structure of a unique admixed population: implications for medical research. *Hum Mol Genet*. 2010;19(3):411-419. doi:10.1093/hmg/ddp505

29. Li Z, Allingham RR, Nakano M, et al; ICAARE-Glaucoma Consortium; NEIGHBORHOOD Consortium. A common variant near TGFBR3 is associated with primary open angle glaucoma. *Hum Mol Genet*. 2015;24(13):3880-3892. doi:10.1093/hmg/ddv128

30. Bailey JN, Loomis SJ, Kang JH, et al; ANZRAG Consortium. Genome-wide association analysis identifies TXNRD2, ATXN2, and FOXC1 as susceptibility loci for primary open-angle glaucoma. *Nat Genet*. 2016;48(2):189-194. doi:10.1038/ng.3482

31. Gharahkhani P, Burdon KP, Fogarty R, et al; Wellcome Trust Case Control Consortium 2, NEIGHBORHOOD consortium. Common variants near ABCA1, AFAP1, and GMDS confer risk of primary open-angle glaucoma. *Nat Genet*. 2014;46(10):1120-1125. doi:10.1038/ng.3079

32. Hunter-Zinck H, Shi Y, Li M, et al; VA Million Veteran Program. Genotyping array design and data quality control in the Million Veteran Program. *Am J Hum Genet*. 2020;106(4):535-548. doi:10.1016/j.ajhg.2020.03.004

33. Fang H, Hui Q, Lynch J, et al; VA Million Veteran Program. Harmonizing genetic ancestry and self-identified race/ethnicity in genome-wide association studies. *Am J Hum Genet*. 2019;105(4):763-772. doi:10.1016/j.ajhg.2019.08.012

34. Auton A, Brooks LD, Durbin RM, et al; The 1000 Genomes Project Consortium. A global reference for human genetic variation. *Nature*. 2015;526(7571):68-74. doi:10.1038/nature15393

35. O'Connell J, Yun T, Moreno M, et al; 23andMe Research Team. A population-specific reference panel for improved genotype imputation in African Americans. *Commun Biol*. 2021;4(1):1269. doi:10.1038/s42003-021-02777-9

36. Foster PJ, Buhrmann R, Quigley HA, Johnson GJ. The definition and classification of glaucoma in prevalence surveys. *Br J Ophthalmol*. 2002;86(2):238-242. doi:10.1136/bjo.86.2.238

37. Hauser MA, Allingham RR, Aung T, et al; Genetics of Glaucoma in People of African Descent (GGLAD) Consortium. Association of genetic variants with primary open-angle glaucoma among individuals with African Ancestry. *JAMA*. 2019;322(17):1682-1691. doi:10.1001/jama.2019.16161

38. Fihn SD, Francis J, Clancy C, et al. Insights from advanced analytics at the Veterans Health Administration. *Health Aff (Millwood)*. 2014;33(7):1203-1211. doi:10.1377/hlthaff.2014.0054

39. Nealon CL, Halladay CW, Kinzy TG, et al; VA Million Veteran Program. Development and evaluation of a rules-based algorithm for primary open-angle glaucoma in the VA Million Veteran Program. *Ophthalmic Epidemiol*. 2022;29(6):640-648. doi:10.1080/09286586.2021.1992784

40. Chang CC, Chow CC, Tellier LC, Vattikuti S, Purcell SM, Lee JJ. Second-generation PLINK: rising to the challenge of larger and richer datasets. *Gigascience*. 2015;4(1):7. doi:10.1186/s13742-015-0047-8

41. Gharahkhani P, Jorgenson E, Hysi P, et al; NEIGHBORHOOD consortium; ANZRAG consortium; Biobank Japan project; FinnGen study; UK Biobank Eye and Vision Consortium; GIGA study group; 23 and Me Research Team. Genome-wide meta-analysis identifies 127 open-angle glaucoma loci with consistent effect across ancestries. *Nat Commun*. 2021;12(1):1258. doi:10.1038/s41467-020-20851-4

42. Nagelkerke NJD. A note on a general definition of the coefficient of determination. *Biometrika*. 1991;78(3):691-692. doi:10.1093/biomet/78.3.691

43. Lee SH, Goddard ME, Wray NR, Visscher PM. A better coefficient of determination for genetic profile analysis. *Genet Epidemiol*. 2012;36(3):214-224. doi:10.1002/gepi.21614

44. Zhang N, Wang J, Li Y, Jiang B. Prevalence of primary open angle glaucoma in the last 20 years: a meta-analysis and systematic review. *Sci Rep*. 2021;11(1):13762. doi:10.1038/s41598-021-92971-w

45. Hingorani AD, Gratton J, Finan C, et al. Performance of polygenic risk scores in screening, prediction, and risk stratification: secondary analysis of data in the Polygenic Score Catalog. *BMJ Med*. 2023;2(1):e000554. doi:10.1136/bmjmed-2023-000554

46. Sud A, Horton RH, Hingorani AD, et al. Realistic expectations are key to realising the benefits of polygenic scores. *BMJ*. 2023;380:e073149. doi:10.1136/bmj-2022-073149

47. Hoffmann TJ, Tang H, Thornton TA, et al. Genome-wide association and admixture analysis of glaucoma in the Women's Health Initiative. *Hum Mol Genet*. 2014;23(24):6634-6643. doi:10.1093/hmg/ddu364

48. Kachuri L, Chatterjee N, Hirbo J, et al; Polygenic Risk Methods in Diverse Populations (PRIMED) Consortium Methods Working Group. Principles and methods for transferring polygenic risk scores across global populations. *Nat Rev Genet*. 2024;25(1):8-25. doi:10.1038/s41576-023-00637-2

49. Rotimi CN, Bentley AR, Doumatey AP, Chen G, Shriner D, Adeyemo A. The genomic landscape of African populations in health and disease. *Hum Mol Genet*. 2017;26(R2):R225-R236. doi:10.1093/hmg/ddx253

50. Sirugo G, Williams SM, Tishkoff SA. The missing diversity in human genetic studies. *Cell*. 2019;177(1):26-31. doi:10.1016/j.cell.2019.02.048

51. Budenz DL, Barton K, Whiteside-de Vos J, et al; Tema Eye Survey Study Group. Prevalence of glaucoma in an urban West African population: the Tema Eye Survey. *JAMA Ophthalmol*. 2013;131(5):651-658. doi:10.1001/jamaophthalmol.2013.1686

52. Verma SS, Gudiseva HV, Chavali VRM, et al; Regeneron Genetics Center; VA Million Veteran Program. A multicohort genome-wide association study in African ancestry individuals reveals risk loci for primary open-angle glaucoma. *Cell*. 2024;187(2):464-480.e10. doi:10.1016/j.cell.2023.12.006

© 2024 American Medical Association. All rights reserved, including those for text and data mining, AI training, and similar technologies.

Supplementary Online Content

Chang-Wolf JM, Kinzy TG, Driessen SJ, et al; GIGA Study Group; GGLAD Study Group; MVP Study Group. Performance of polygenic risk scores for primary open-angle glaucoma in populations of African descent. *JAMA Ophthalmol*. Published online November 14, 2024. doi:10.1001/jamaophthalmol.2024.4784

eFigure 1. Density Distributions

eTable 1. Highest Quintile Odds Ratios

eFigure 2. Case Proportions by Quintile

eTable 2. Area Under the Receiver Operating Characteristic Curve

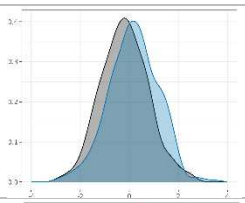
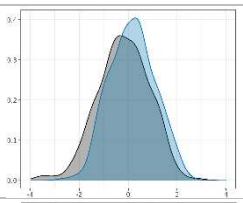
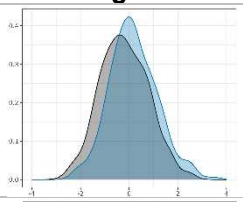
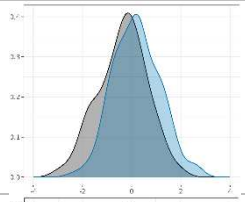
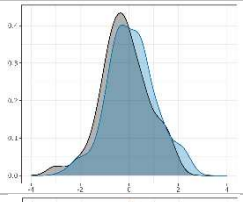
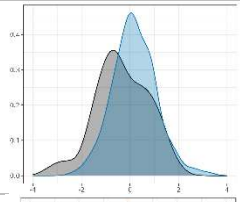
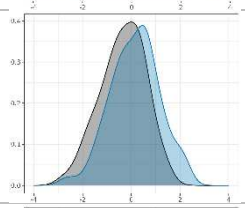
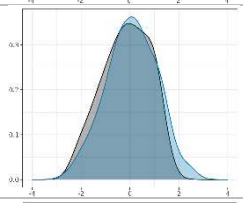
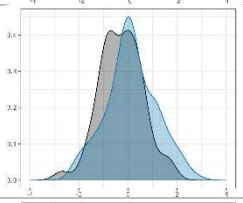
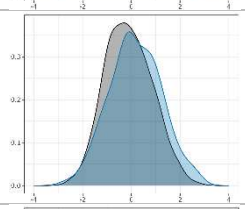
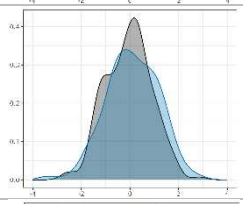
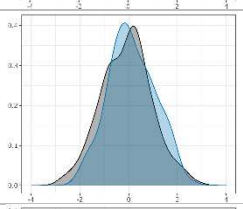
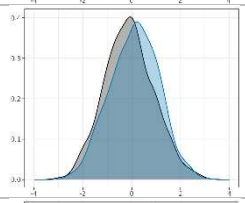
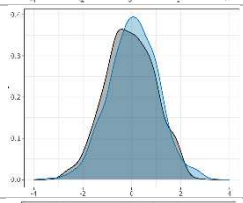
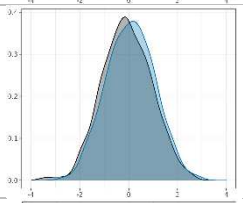
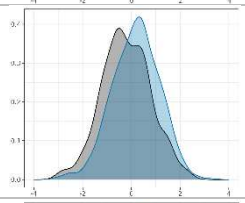
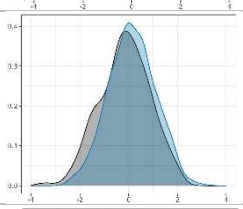
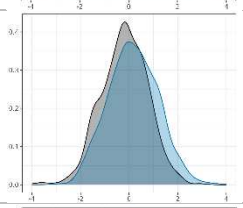
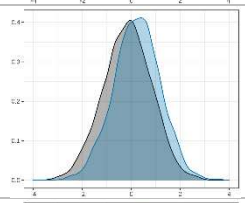
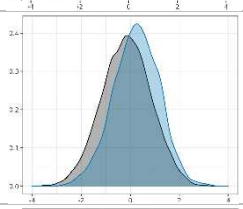
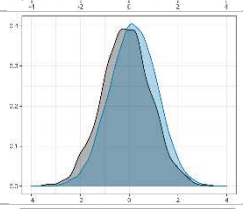
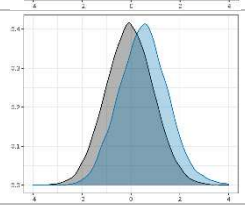
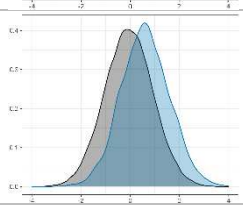
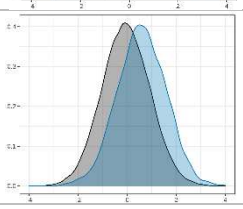
eTable 3. R^2 Values

eTable 4. Linkage Disequilibrium Proxy Polygenic Risk Score Results

This supplementary material has been provided by the authors to give readers additional information about their work.

© 2024 American Medical Association. All rights reserved.

eFigure 1. Density distributions. This figure displays the density distributions for the 3 polygenic risk scores (PRSs) in each of the 8 study groups. Controls are depicted in grey, and cases in blue.

Group	Gharahkhani-PRS	Han-PRS	Craig-PRS
Tanzanian			
South African Coloured			
South African Black			
Nigerian			
Ghanaian			
African American (Eyes of Africa)			
African American (Million Veteran Program)			
European			

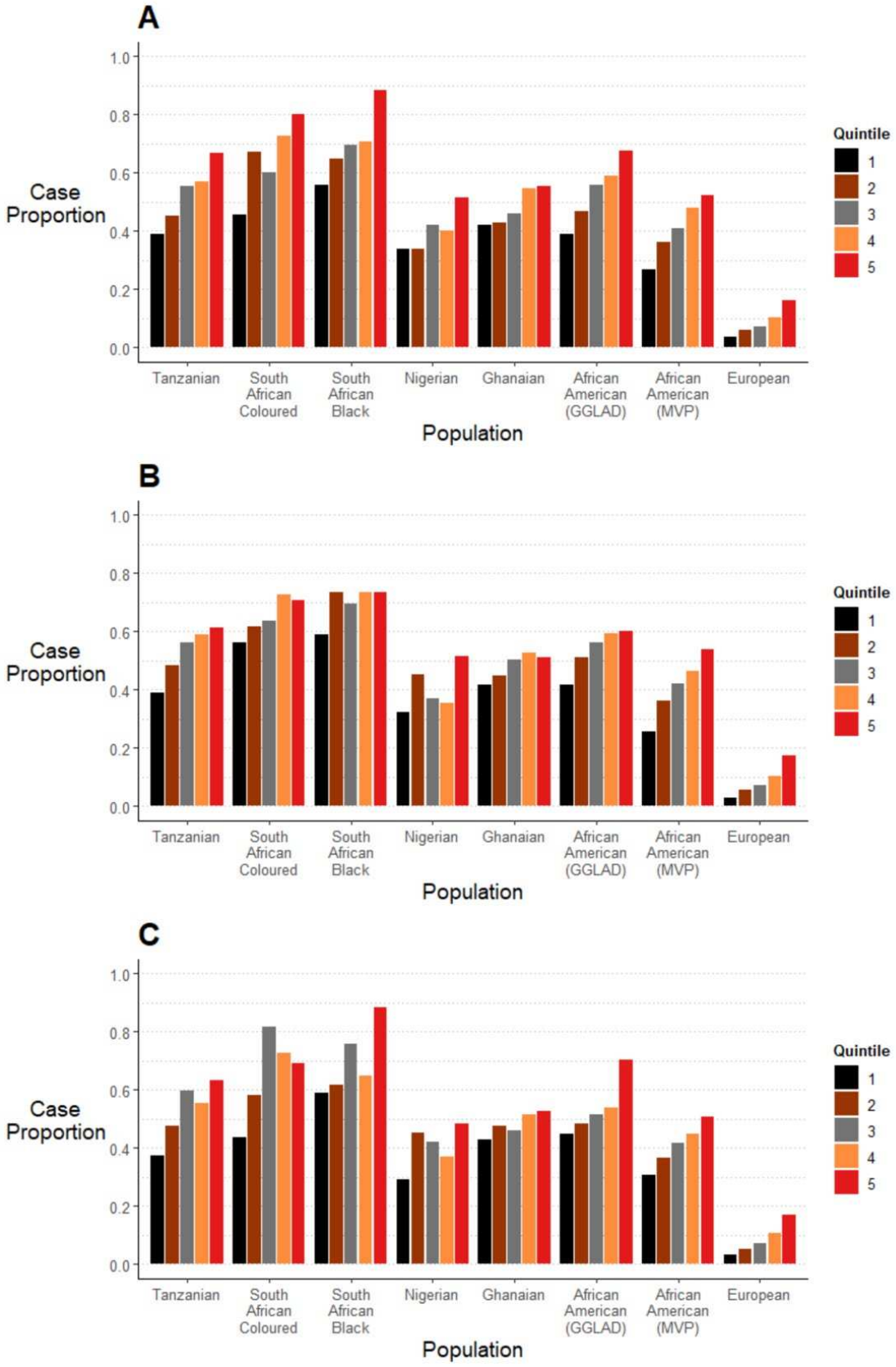
© 2024 American Medical Association. All rights reserved.

eTable 1. Highest quintile odds ratios (ORs). This table displays the ORs and 95% confidence intervals (in parentheses) of the highest quintile compared to the lowest quintile of primary open-angle glaucoma risk for each of the 3 polygenic risk scores (PRSs) in the 8 study groups. Models were adjusted for age, sex, and the 1st 5 principal components. *P*-values lower than .05 are provided. Additional abbreviations: GGLAD = Genetics of Glaucoma in People of African Descent. MVP = Million Veteran Program.

	Tanzanian	South African Coloured	South African Black	Nigerian	Ghanaian	African American (GGLAD)	African American (MVP)	European
Gharahkhani-PRS	3.37 (1.98-5.79) *P* < .001	7.05 (2.73-19.6) *P* < .001	5.89 (1.72-24.3) *P* = .008	1.96 (.939-4.14)	1.68 (1.17-2.43) *P* = .005	4.00 (2.60-6.22) *P* < .001	2.47 (2.14-2.86) *P* < .001	5.02 (4.54-5.57) *P* < .001
Han-PRS	2.72 (1.63-4.58) *P* < .001	2.11 (.90-5.08)	1.93 (.64-6.06)	2.09 (.989-4.51)	1.63 (1.13-2.35) *P* = .009	2.27 (1.49-3.47) *P* < .001	2.91 (2.52-3.37) *P* < .001	7.24 (6.47-8.12) *P* < .001
Craig-PRS	3.24 (1.94-5.47) *P* < .001	3.68 (1.62-8.61) *P* = .002	4.51 (1.31-18.6) *P* = .023	2.21 (1.03-4.83) *P* = .044	1.51 (1.05-2.18) *P* = .028	2.95 (1.94-4.53) *P* < .001	2.07 (1.81-2.39) *P* < .001	6.31 (5.67-7.04), *P* < .001

© 2024 American Medical Association. All rights reserved.

eFigure 2. Case Proportions by Quintile. This figure presents case proportions for different populations and quintiles within each of three polygenic risk score (PRS) types: A. Gharahkhani-PRS, B. Han-PRS, and C. Craig-PRS. Each bar plot showcases case proportions in various populations, with quintiles distinguished by different fill colors. The y-axis represents the case proportion, and the x-axis displays the population. Additional abbreviations: GGLAD = Genetics of Glaucoma in People of African Descent. MVP = Million Veteran Program.



© 2024 American Medical Association. All rights reserved.

eTable 2. Area under the receiver operating characteristic curve (AUC). This table displays AUCs and 95% confidence intervals (in parentheses) for each of the 3 polygenic risk scores (PRSs) in the 8 study groups. *P*-values below .05 are given to indicate the difference in AUC compared to a baseline model (age, sex, and first 5 principal components) identified using DeLong's ROC test. Additional abbreviations: GGLAD = Genetics of Glaucoma in People of African Descent. MVP = Million Veteran Project.

	Age + sex + PCs (baseline)	Baseline + Gharahkhani-PRS	Baseline + Han-PRS	Baseline + Craig-PRS
Tanzanian	.659 (.619-.700)	.685 (.646-.724) *P* = .033	.687 (.648-.726) *P* = .019	.694 (.655-.733) *P* = .007
South African Coloured	.588 (.520-.656)	.689 (.625-.752) *P* = .008	.611 (.542-.679)	.669 (.602-.735) *P* = .027
South African Black	.707 (.630-.785)	.752 (.679-.826)	.720 (.643-.797)	.741 (.665-.818)
Nigerian	.619 (.556-.682)	.639 (.576-.701)	.624 (.561-.687)	.627 (.564-.690)
Ghanaian	.705 (.677-.734)	.712 (.684-.740)	.710 (.682-.738)	.710 (.682-.738)
African American (GGLAD)	.813 (.790-.836)	.83 (.808-.852) *P* < .001	.822 (.800-.845) *P* = .005	.825 (.802-.847) *P* = .002
African American (MVP)	.688 (.677-.699)	.704 (.693-.715) *P* < .001	.706 (.695-.717) *P* < .001	.698 (.687-.709) *P* < .001
European	.522 (.514-.530)	.661 (.654-.669) *P* < .001	.686 (.679-.693) *P* < .001	.680 (.673-.688) *P* < .001

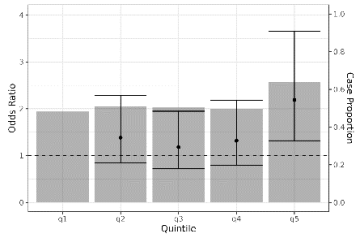
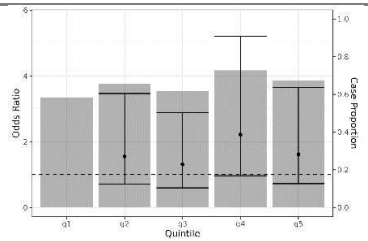
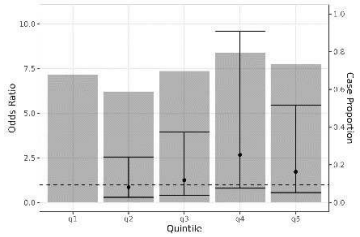
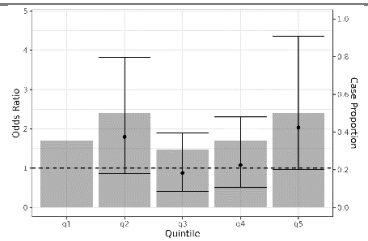
© 2024 American Medical Association. All rights reserved.

eTable 3. R^2 values: Performance evaluation of the 3 polygenic risk scores (PRSs) for the 8 study groups regarding R-squared (R^2) values on the observed and liability scales. For liability scale calculations, we used 2.4% as a fixed prevalence value for POAG (Zhang et al. 2021) and case proportions (cp) per group. Additional abbreviations: GGLAD = Genetics of Glaucoma in People of African Descent. MVP = Million Veteran Project. SNP = Single-nucleotide polymorphism.

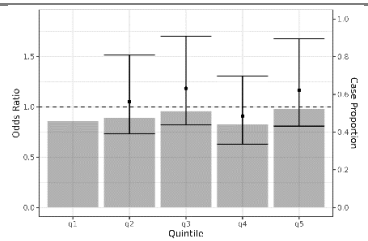
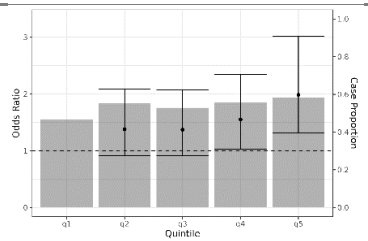
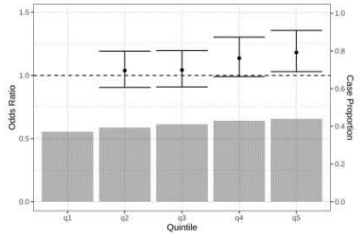
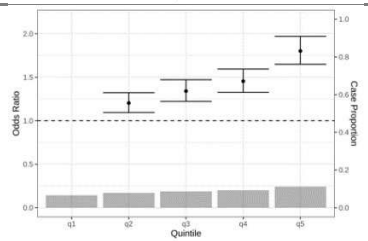
LIABILITY R^2	**Tanzanian** cp = .5266	**South African Coloured** cp = .6509	**South African Black** cp = .6982	**Nigerian** cp = .4032	**Ghanaian** cp = .4812	**African American (GGLAD)** cp = .5377	**African American (MVP)** cp = .4090	**European** cp = .0872
Age + sex	.026	.005	.050	.012	.028	.115	.069	.002
Age + sex + 5 PCs	.029	.011	.069	.018	.047	.121	.078	.002
R^2 for each PRS below is based on its addition to age + sex + 5 PCs.								
Gharahkhani-PRS	.012	.032	.026	.007	.004	.015	.016	.057
Han-PRS	.012	.008	.005	.002	.002	.008	.019	.077
Craig-PRS	.013	.026	.017	.004	.002	.012	.010	.071

© 2024 American Medical Association. All rights reserved.

eTable 4. Linkage disequilibrium (LD) proxy polygenic risk score (PRS) results. This table displays odds ratios (ORs) and case proportions (CPs) by quintile, including OR of risk in the highest quintile, as well as areas under the curve (AUCs) and $R^{2,}$ increases over baseline (age + sex + 1st 5 principal components) for the LD proxy PRS. 95% confidence intervals (in parentheses) and *P*-values are provided when below a value .05.

Group	ORs and CPs by quintile	Highest quintile OR	AUC	Liability R^2 increase
Tanzanian		2.19 (1.32-3.66) *P* = .003	.672 (.633-.712)	.00363
South African Coloured		1.61 (.723-3.64)	.592 (.522-.662)	.001029
South African Black		1.72 (.557-5.46)	.719 (.642-.795)	.002971
Nigerian		2.04 (.967-4.36)	.625 (.562-.688)	.000501

© 2024 American Medical Association. All rights reserved.

Group	ORs and CPs by quintile	Highest quintile OR	AUC	Liability R^2 increase
Ghanaian		1.16 (.809-1.67)	.706 (.677-.734)	.000303
African American (Genetics of Glaucoma in individuals of African Descent)		1.98 (1.31-3.02) *P* = .001	.817 (.794-.840)	.002034
African American (Million Veteran Project)		1.18 (1.03-1.36) *P* = .017	.689 (.677-.700)	.000777
European		1.8 (1.65-1.97) *P* < .001	.566 (.558-.574) *P* < .001	.008574

© 2024 American Medical Association. All rights reserved.

Supplemental Online Content: Nonauthor Collaborators
*First name, last name, and suffix (if applicable) are required and will appear in PubMed.

***Group Name(s): Genetics in Glaucoma Patients of African Descent (GIGA) Study Group, Genetics of Glaucoma in People of African Descent (GGLAD) Study Group, Million Veteran Program (MVP), and Cooperative Studies Program (CSP) #572**							
***First Name and Middle Initial(s)**	***Last Name**	***Suffix (eg, Jr, III)**	Academic Degrees	Institution	Location (city, state/province, country)	Role or Contribution, eg, chair, principal investigator	Group (if more than 1 Group listed in the byline) and/or Subgroup (eg, Steering Committee)
Anna J.	Sanywia		MD, MPH	Department of Ophthalmology Muhimbili University of Health and Allies Sciences	Dar es Salaam, Tanzania		Genetics in glaucoma patients of African descent (GIGA)
Colin	Cook		MD, PhD	Division of Ophthalmology, University of Cape Town,	Cape Town, South Africa		Genetics in glaucoma patients of African descent (GIGA)
Hassan G.	Hassan		MD	Department of Ophthalmology, Comprehensive Community Based Rehabilitation in Tanzania (CCBRT) Hospital	Dar es Salaam, Tanzania		Genetics in glaucoma patients of African descent (GIGA)
Neema	Kanyaro		MD	Department of Ophthalmology Muhimbili University of Health and Allies Sciences	Dar es Salaam, Tanzania		Genetics in glaucoma patients of African descent (GIGA)
Cyprian	Ntomoka		MD	Department of Ophthalmology, Comprehensive Community Based Rehabilitation in Tanzania (CCBRT) Hospital	Dar es Salaam, Tanzania		Genetics in glaucoma patients of African descent (GIGA)
R.R.	Allingham		MD	Department of Ophthalmology, Duke University, Durham, NC & Singapore Eye Research Institute, Singapore	Durham, NC		Genetics of Glaucoma in People of African Descent (GGLAD)
Carly J	van der Heide		MD	Department of Opthalmology, University of Iowa	University of Iowa		Genetics of Glaucoma in People of African Descent (GGLAD)

Supplemental Online Content: Nonauthor Collaborators
*First name, last name, and suffix (if applicable) are required and will appear in PubMed.

***First Name and Middle Initial(s)**	***Last Name**	***Suffix (eg, Jr, III)**	Academic Degrees	Institution	Location (city, state/province, country)	Role or Contribution, eg, chair, principal investigator	Group (if more than 1 Group listed in the byline) and/or Subgroup (eg, Steering Committee)
Kent D	Taylor		PhD	Institute for Translational Genomics and Population Sciences, Los Angeles Biomedical Research Institute, UCLA, CA & Department of Pediatrics, Harbor-University of California, Los Angeles Medical Center, Torrance, California	Los Angeles, CA		Genetics of Glaucoma in People of African Descent (GGLAD)
Jerome I	Rotter		MD, PhD	Institute for Translational Genomics and Population Sciences, Los Angeles Biomedical Research Institute, UCLA, CA	Los Angeles, CA		Genetics of Glaucoma in People of African Descent (GGLAD)
Shih-Hsiu J	Wang		MD, PhD	Department of Pathology, Duke University, Durham, NC	Durham, NC		Genetics of Glaucoma in People of African Descent (GGLAD)
Sadiq M	ABDULLAHI		MD	National Eye Centre, Kaduna, Nigeria,West Africa	Kaduna, Nigeria, West Africa		Genetics of Glaucoma in People of African Descent (GGLAD)
Khaled K.	Abu-Amero		PhD	Department of Ophthalmology, College of Medicine, King Saud University, Riyadh 11411, Saudi Arabia	Riyadh 11411, Saudi Arabia		Genetics of Glaucoma in People of African Descent (GGLAD)
Michael G	Anderson		PhD	Department of Ophthalmology and Visual Sciences, Carver College of Medicine, University of Iowa, Iowas City, IA	Iowa City, IA		Genetics of Glaucoma in People of African Descent (GGLAD)
Stephen	Akafo		MB ChB, FWACS	Unit of Ophthalmology, Department of Surgery, University of Ghana Medical School, Accra, Ghana	Accra, Ghana		Genetics of Glaucoma in People of African Descent (GGLAD)

Supplemental Online Content: Nonauthor Collaborators
*First name, last name, and suffix (if applicable) are required and will appear in PubMed.

***First Name and Middle Initial(s)**	***Last Name**	***Suffix (eg, Jr, III)**	Academic Degrees	Institution	Location (city, state/province, country)	Role or Contribution, eg, chair, principal investigator	Group (if more than 1 Group listed in the byline) and/or Subgroup (eg, Steering Committee)
Mahmoud B	ALHASSAN		MD	National Eye Centre, Kaduna, Nigeria,West Africa	Kaduna, Nigeria, West Africa		Genetics of Glaucoma in People of African Descent (GGLAD)
Ifeoma	Asimadu		MBBS	Department of Ophthalmology, ESUT Teaching Hospital Parklane, Enugu,Nigeria	Enugu, Nigeria		Genetics of Glaucoma in People of African Descent (GGLAD)
Radha	Ayyagari		PhD	Shiley Eye Institute, Department of Ophthalmology,University of California San Diego, La Jolla, California	La Jolla, California		Genetics of Glaucoma in People of African Descent (GGLAD)
Seydou	BAKAYOKO		MD	Institut d'Ophtalmologie Tropicale de l'Afrique, Bamako, Mali & Université des sciences des techniques et des technologies de Bamako	Bamako, Mali		Genetics of Glaucoma in People of African Descent (GGLAD)
Prisca	BIANGOUP NYAMSI		MD	Service spécialisé d'ophtalmologie, Hôpital Militaire de Région N°1 de Yaoundé, Yaoundé; Cameroun	Yaoundé, Cameroun		Genetics of Glaucoma in People of African Descent (GGLAD)
Donald W	Bowden		PhD	Department of Biochemistry; Center for Diabetes Research; Wake Forest School of Medicine, Winston-Salem, NC	Winston-Salem, NC		Genetics of Glaucoma in People of African Descent (GGLAD)
William C	Bromley		MD	Center for Human Genetics, Bar Harbor, ME	Bar Harbor, ME		Genetics of Glaucoma in People of African Descent (GGLAD)
Donald L	Budenz		MD, MPH	Department of Ophthalmology, University of North Carolina, Chapel Hill, NC, US	Chapel Hill, NC, US		Genetics of Glaucoma in People of African Descent (GGLAD)

Supplemental Online Content: Nonauthor Collaborators
*First name, last name, and suffix (if applicable) are required and will appear in PubMed.

***First Name and Middle Initial(s)**	***Last Name**	***Suffix (eg, Jr, III)**	Academic Degrees	Institution	Location (city, state/province, country)	Role or Contribution, eg, chair, principal investigator	Group (if more than 1 Group listed in the byline) and/or Subgroup (eg, Steering Committee)
Trevor R	Carmichael		MBBCh, FCS (SA)	Division of Ophthalmology, Department of Neurosciences, University of the Witwatersrand, Johannesburg, South Africa	Johannesburg, South Africa		Genetics of Glaucoma in People of African Descent (GGLAD)
Pratap	Challa		MD	Department of Ophthalmology, Duke University, Durham, NC	Durham, NC		Genetics of Glaucoma in People of African Descent (GGLAD)
Yii-Der Ida	Chen		PhD	Institute for Translational Genomics and Population Sciences, Los Angeles Biomedical Research Institute, UCLA, CA & Department of Pediatrics, Harbor-University of California, Los Angeles Medical Center, Torrance, California	Los Angeles, CA		Genetics of Glaucoma in People of African Descent (GGLAD)
Chimdi M	Chuka-Okosa		MBBS, FWACS, MSc	Department of Ophthalmology, University of Nigeria, Ituku, Nigeria	Ituku, Nigeria		Genetics of Glaucoma in People of African Descent (GGLAD)
Vital Paulino	Costa		MD, PhD	Department of Ophthalmology, Faculty of Medical Sciences, University of Campinas , Campinas, SP, Brazil	Campinas, SP, Brazil		Genetics of Glaucoma in People of African Descent (GGLAD)
Dianne A	Cruz		MD	Department of Psychiatry and Behavioral Sciences, Duke University, Durham, NC, US	Durham, NC, US		Genetics of Glaucoma in People of African Descent (GGLAD)
Harvey	DuBiner		MD	Clayton Eye Care Center Management, Inc., Marrow, Georgia 30260, USA	Marrow, Georgia 30260, USA		Genetics of Glaucoma in People of African Descent (GGLAD)

Supplemental Online Content: Nonauthor Collaborators
*First name, last name, and suffix (if applicable) are required and will appear in PubMed.

***First Name and Middle Initial(s)**	***Last Name**	***Suffix (eg, Jr, III)**	Academic Degrees	Institution	Location (city, state/province, country)	Role or Contribution, eg, chair, principal investigator	Group (if more than 1 Group listed in the byline) and/or Subgroup (eg, Steering Committee)
JF	Ervin		MD	Kathleen Price Bryan Brain Bank and Biorepository , Department of Neurology, Duke University, Durham, NC, US	Durham, NC, US		Genetics of Glaucoma in People of African Descent (GGLAD)
Robert M	Feldman		MD	Ruiz Department of Ophthalmology & Visual Science, McGovern Medical School, The University of Texas Health Science Center at Houston, Houston, Texas	Houston, Texas		Genetics of Glaucoma in People of African Descent (GGLAD)
Miles	Flamme-Wiese		MD	Department of Ophthalmology and Visual Sciences, Carver College of Medicine, University of Iowa, Iowas City, IA	Iowa City, IA		Genetics of Glaucoma in People of African Descent (GGLAD)
Douglas E	Gaasterland		PhD	The Emmes Corporation, Rockville, MD, US	Rockville, MD, US		Genetics of Glaucoma in People of African Descent (GGLAD)
Sarah	Garnai		PhD	Department of Ophthalmology and Visual Sciences, University of Michigan, Ann Arbor, MI	Ann Arbor, MI		Genetics of Glaucoma in People of African Descent (GGLAD)
Christopher A	Girkin		MD, PhD	Department of Ophthalmology and Visual Sciences, University of Alabama Birmingham, Birmingham, AL, US	Birmingham, AL, US		Genetics of Glaucoma in People of African Descent (GGLAD)
Nouhoum	GUIROU		MD	Institut d'Ophtalmologie Tropicale de l'Afrique, Bamako, Mali & Université des sciences des techniques et des technologies de Bamako	Bamako, Mali		Genetics of Glaucoma in People of African Descent (GGLAD)

Supplemental Online Content: Nonauthor Collaborators
*First name, last name, and suffix (if applicable) are required and will appear in PubMed.

***First Name and Middle Initial(s)**	***Last Name**	***Suffix (eg, Jr, III)**	Academic Degrees	Institution	Location (city, state/province, country)	Role or Contribution, eg, chair, principal investigator	Group (if more than 1 Group listed in the byline) and/or Subgroup (eg, Steering Committee)
Xiuqing	Guo		PhD	Institute for Translational Genomics and Population Sciences, Los Angeles Biomedical Research Institute, UCLA, CA & Department of Pediatrics, Harbor-University of California, Los Angeles Medical Center, Torrance, California	Los Angeles, CA		Genetics of Glaucoma in People of African Descent (GGLAD)
Jonathan	Haines		PhD	Department of Population and Quantitative Health Sciences, Case Western Reserve University, Cleveland, OH, US & Institute for Computational Biology, Case Western Reserve University, Cleveland, OH, US	Cleveland, OH, US		Genetics of Glaucoma in People of African Descent (GGLAD)
CJ	Hammond		MD, PhD	Section of Academic Ophthalmology, School of Life Course Sciences, FoLSM, King's College London, London, United Kingdom	London, United Kingdom		Genetics of Glaucoma in People of African Descent (GGLAD)
Leon	Herndon		MD	Department of Ophthalmology, Duke University, Durham, NC	Durham, NC		Genetics of Glaucoma in People of African Descent (GGLAD)
Thomas J	Hoffmann		PhD	Department of Epidemiology and Biostatistics, University of California San Francisco, San Francisco, CA & Institute for Human Genetics, University of California San Francisco, San Francisco, CA	San Francisco, CA		Genetics of Glaucoma in People of African Descent (GGLAD)
Christine M	Hulette		MD	Department of Pathology, Duke University, Durham, NC	Durham, NC		Genetics of Glaucoma in People of African Descent (GGLAD)

Supplemental Online Content: Nonauthor Collaborators
*First name, last name, and suffix (if applicable) are required and will appear in PubMed.

***First Name and Middle Initial(s)**	***Last Name**	***Suffix (eg, Jr, III)**	Academic Degrees	Institution	Location (city, state/province, country)	Role or Contribution, eg, chair, principal investigator	Group (if more than 1 Group listed in the byline) and/or Subgroup (eg, Steering Committee)
Abba	Hydara		MD	Sheikh Zayed Regional Eye Care Centre, Kanifing, The Gambia	Kanifing, The Gambia		Genetics of Glaucoma in People of African Descent (GGLAD)
Robert P	Igo Jr.		PhD	Department of Population and Quantitative Health Sciences, Case Western Reserve University, Cleveland, OH, US	Cleveland, OH, US		Genetics of Glaucoma in People of African Descent (GGLAD)
Eric	Jorgenson		PhD	Kaiser Permanente Northern California (KPNC), Division of Research, Oakland, CA, US	Oakland, CA, US		Genetics of Glaucoma in People of African Descent (GGLAD)
Joyce	KABWE		MD	Department of Ophthalmology, Saint Joseph Hospital, Kinshasa, Limete, Democratic Republic of the Congo	Kinshasa, Limete, Democratic Republic of the Congo		Genetics of Glaucoma in People of African Descent (GGLAD)
Ngoy Janvier	KILANGALANGA		MD	Department of Ophthalmology, Saint Joseph Hospital, Kinshasa, Limete, Democratic Republic of the Congo	Kinshasa, Limete, Democratic Republic of the Congo		Genetics of Glaucoma in People of African Descent (GGLAD)
Nkiru	Kizor-Akaraiwe		MD	Department of Ophthalmology, ESUT Teaching Hospital Parklane, Enugu,Nigeria & The Eye Specialists Hospital, Enugu, Nigeria	Enugu, Nigeria		Genetics of Glaucoma in People of African Descent (GGLAD)
Rachel W	Kuchtey		MD, PhD	Department of Ophthalmology and Visual Sciences, Vanderbilt University Medical Center, Nashville, TN	Nashville, TN		Genetics of Glaucoma in People of African Descent (GGLAD)
Hasnaa	LAMARI		MD	Clinique Spécialisée en Ophtalmologie Mohammedia, Mohammedia, Morocco	Mohammedia, Morocco		Genetics of Glaucoma in People of African Descent (GGLAD)
Zheng	Li		MD, PhD	Genome Institutue of Singapore, Singapore	Singapore		Genetics of Glaucoma in People of African Descent (GGLAD)

Supplemental Online Content: Nonauthor Collaborators
*First name, last name, and suffix (if applicable) are required and will appear in PubMed.

***First Name and Middle Initial(s)**	***Last Name**	***Suffix (eg, Jr, III)**	Academic Degrees	Institution	Location (city, state/province, country)	Role or Contribution, eg, chair, principal investigator	Group (if more than 1 Group listed in the byline) and/or Subgroup (eg, Steering Committee)
Jeffrey M	Liebmann		MD, PhD	Bernard and Shirlee Brown Glaucoma Research Laboratory, Harkness Eye Institute, Columbia University Medical Center, New York, New York	New York, New York		Genetics of Glaucoma in People of African Descent (GGLAD)
Yutao	Liu		MD	Cellular Biology and Anatomy, Augusta University, Augusta, GA & James & Jean Culver Vision Discovery Institute, Augusta University, Augusta, GA & Center for Biotechnology & Genomic Medicine, Augusta University, Augusta, GA	Augusta, GA		Genetics of Glaucoma in People of African Descent (GGLAD)
Ruth JF	Loos		MD	The Charles Bronfman Institute for Personalized Medicine, Icahn School of Medicine at Mount Sinai, New York, New York & The Mindich Child Health and Development Institute, Icahn School of Medicine at Mount Sinai, New York, New York	New York, New York		Genetics of Glaucoma in People of African Descent (GGLAD)
Monica B	Melo		MD	Center of Molecular Biology and Genetic Engineering, University of Campinas, Campinas, SP, Brazil	Campinas, SP, Brazil		Genetics of Glaucoma in People of African Descent (GGLAD)
Sayoko E	Moroi		MD, PhD	Department of Ophthalmology and Visual Sciences, University of Michigan, Ann Arbor, MI	Ann Arbor, MI		Genetics of Glaucoma in People of African Descent (GGLAD)
Joseph M	Msosa		MD	Lions Sight-First Eye Hospital, Kamuzu Central Hospital, Lilongwe, Malawi	Lilongwe, Malawi		Genetics of Glaucoma in People of African Descent (GGLAD)

Supplemental Online Content: Nonauthor Collaborators
*First name, last name, and suffix (if applicable) are required and will appear in PubMed.

***First Name and Middle Initial(s)**	***Last Name**	***Suffix (eg, Jr, III)**	Academic Degrees	Institution	Location (city, state/province, country)	Role or Contribution, eg, chair, principal investigator	Group (if more than 1 Group listed in the byline) and/or Subgroup (eg, Steering Committee)
Robert F	Mullins		MD	Department of Ophthalmology and Visual Sciences, Carver College of Medicine, University of Iowa, Iowas City, IA	Iowa City, IA		Genetics of Glaucoma in People of African Descent (GGLAD)
Girish	Nadkarni		MD	The Charles Bronfman Institute for Personalized Medicine, Icahn School of Medicine at Mount Sinai, New York, New York & Division of Nephrology, Department of Medicine, Icahn School of Medicine at Mount Sinai, New York	New York, New York		Genetics of Glaucoma in People of African Descent (GGLAD)
Abdoulaye	NAPO		MD	Institut d'Ophtalmologie Tropicale de l'Afrique, Bamako, Mali & Université des sciences des techniques et des technologies de Bamako,Bamako, Mali	Bamako, Mali		Genetics of Glaucoma in People of African Descent (GGLAD)
Maggie C.Y.	Ng		MD	Department of Biochemistry, Center for Diabetes Research, Wake Forest School of Medicine, Winston-Salem, NC	Winston-Salem, NC		Genetics of Glaucoma in People of African Descent (GGLAD)
Hugo Freire	Nunes		MD	Center for Molecular Biology and Genetic Engineering, University of Campinas , Campinas, Brazil	Campinas, Brazil		Genetics of Glaucoma in People of African Descent (GGLAD)
Ebenezer	Obeng-Nyarkoh		MD	Center for Human Genetics, Bar Harbor, ME	Bar Harbor, ME		Genetics of Glaucoma in People of African Descent (GGLAD)
Anthony	Okeke		MD	Nigerian Navy Reference Hospital, Ojo, Lagos, Nigeria	Ojo, Lagos, Nigeria		Genetics of Glaucoma in People of African Descent (GGLAD)

Supplemental Online Content: Nonauthor Collaborators
*First name, last name, and suffix (if applicable) are required and will appear in PubMed.

***First Name and Middle Initial(s)**	***Last Name**	***Suffix (eg, Jr, III)**	Academic Degrees	Institution	Location (city, state/province, country)	Role or Contribution, eg, chair, principal investigator	Group (if more than 1 Group listed in the byline) and/or Subgroup (eg, Steering Committee)
Suhanya	Okeke		MD	Department of Opthalmology, ESUT Teaching Hospital Parklane, Enugu, Nigeria & The Eye Specialists Hospital, Enugu, Nigeria	Enugu, Nigeria		Genetics of Glaucoma in People of African Descent (GGLAD)
Olusegun	OLANIYI		MD, PhD	National Eye Centre, Kaduna, Nigeria	Kaduna, Nigeria		Genetics of Glaucoma in People of African Descent (GGLAD)
Mariana Borges	Oliveira		MD	Center for Molecular Biology and Genetic Engineering, University of Campinas, Campinas, Brazil	Campinas, Brazil		Genetics of Glaucoma in People of African Descent (GGLAD)
Louis R	Pasquale		PhD	Icahn School of Medicine at Mount Sinai, Department of Ophthalmology, New York, NY & Channing Division of Network Medicine, Brigham and Women's Hospital, Boston, MA	New York, NY		Genetics of Glaucoma in People of African Descent (GGLAD)
Rodolfo A.	Perez-Grossmann		PhD	Instituto de Glaucoma y Catarata, Lima, Perú	Lima, Perú		Genetics of Glaucoma in People of African Descent (GGLAD)
Margaret A	Pericak-Vance		MD, PhD	John P Hussman Institute for Human Genomics. University of Miami Miller School of Medicine, Miami, FL, US	Miami, FL, US		Genetics of Glaucoma in People of African Descent (GGLAD)
XJ	Qin		PhD	Duke Molecular Physiology Institute, Duke University, Durham, NC, US	Durham, NC, US		Genetics of Glaucoma in People of African Descent (GGLAD)

Supplemental Online Content: Nonauthor Collaborators
*First name, last name, and suffix (if applicable) are required and will appear in PubMed.

***First Name and Middle Initial(s)**	***Last Name**	***Suffix (eg, Jr, III)**	Academic Degrees	Institution	Location (city, state/province, country)	Role or Contribution, eg, chair, principal investigator	Group (if more than 1 Group listed in the byline) and/or Subgroup (eg, Steering Committee)
Serge	RESNIKOFF		PhD	Brien Holden Vision Institute, Sydney, Australia & School of Optometry and Vision Science, University of New South Wales, Sydney, Australia	Johannesburg, South Africa		Genetics of Glaucoma in People of African Descent (GGLAD)
Julia E	Richards		MD, PhD	Department of Ophthalmology and Visual Sciences, University of Michigan, Ann Arbor, MI & Department of Epidemiology, University of Michigan, Ann Arbor, MI, US	Ann Arbor, MI		Genetics of Glaucoma in People of African Descent (GGLAD)
Rui Barroso	Schimiti		PhD	Hoftalon Hospital, Londrina, Brazil	Londrina, Brazil		Genetics of Glaucoma in People of African Descent (GGLAD)
Kar Seng	Sim		MD	Genome Institutue of Singapore, Singapore	Singapore		Genetics of Glaucoma in People of African Descent (GGLAD)
William E	Sponsel		MD	Eyes of Africa, Child Legacy International (CLI) Hospital, Msundwe, Malawi & Eyes of Africa, Child Legacy International (CLI) Hospital, Msundwe, Malawi	Msundwe, Malawi		Genetics of Glaucoma in People of African Descent (GGLAD)
Paulo Vinícius	Svidnicki		MD, PhD	Center for Molecular Biology and Genetic Engineering, University of Campinas , Campinas, Brazil	Campinas, Brazil		Genetics of Glaucoma in People of African Descent (GGLAD)
Nkechinyere J	Uche		PhD	Department of Ophthalmology, University of Nigeria Teaching Hospital, Ituku Ozalla, Enugu, Nigeria & The Eye Specialists Hospital, Enugu, Nigeria	Ituku Ozalla, Enugu, Nigeria		Genetics of Glaucoma in People of African Descent (GGLAD)

Supplemental Online Content: Nonauthor Collaborators
*First name, last name, and suffix (if applicable) are required and will appear in PubMed.

***First Name and Middle Initial(s)**	***Last Name**	***Suffix (eg, Jr, III)**	Academic Degrees	Institution	Location (city, state/province, country)	Role or Contribution, eg, chair, principal investigator	Group (if more than 1 Group listed in the byline) and/or Subgroup (eg, Steering Committee)
CM	van Duijn		MD	Department of Epidemiology, Erasmus Medical Center, Rotterdam, The Netherlands	Rotterdam, The Netherlands		Genetics of Glaucoma in People of African Descent (GGLAD)
José Paulo Cabral de	Vasconcellos		MD, PhD	Department of Ophthalmology, Faculty of Medical Sciences, University of Campinas , Campinas, Brazil	Campinas, Brazil		Genetics of Glaucoma in People of African Descent (GGLAD)
Janey L	Wiggs		MD	Harvard, University Medical School, Boston MA, US & Massachusetts Eye and Ear Hospital. Boston MA, US	Boston, MA, US		Genetics of Glaucoma in People of African Descent (GGLAD)
Linda M	Zangwill		PhD	Department of Ophthalmology, Hamilton Glaucoma Center, Shiley Eye Institute, University of California, San Diego, La Jolla, California	La Jolla, California		Genetics of Glaucoma in People of African Descent (GGLAD)
Neil	Risch		MD	Department of Epidemiology and Biostatistics, University of California San Francisco, San Francisco, CA & Institute for Human Genetics, University of California San Francisco, San Francisco, CA & Kaiser Permanente Northern California, Division of Research, Oakland, CA	San Francisco, CA		Genetics of Glaucoma in People of African Descent (GGLAD)
Dan	Milea		PhD	Singapore Eye Research Institute, Singapore	Singapore		Genetics of Glaucoma in People of African Descent (GGLAD)

Supplemental Online Content: Nonauthor Collaborators
*First name, last name, and suffix (if applicable) are required and will appear in PubMed.

***First Name and Middle Initial(s)**	***Last Name**	***Suffix (eg, Jr, III)**	Academic Degrees	Institution	Location (city, state/province, country)	Role or Contribution, eg, chair, principal investigator	Group (if more than 1 Group listed in the byline) and/or Subgroup (eg, Steering Committee)
Robert N	Weinreb		MD, PhD	Shiley Eye Institute, Department of Ophthalmology,University of California San Diego, La Jolla, California	La Jolla, California		Genetics of Glaucoma in People of African Descent (GGLAD)
Allison E	Ashley-Koch		PhD	Department of Medicine, Duke University, Durham, NC	Durham, NC		Genetics of Glaucoma in People of African Descent (GGLAD)
John H	Fingert		MD, PhD	Department of Ophthalmology and Visual Sciences, Carver College of Medicine, University of Iowa, Iowas City, IA	Iowa City, IA		Genetics of Glaucoma in People of African Descent (GGLAD)
Mihaela	Aslan		PhD	Clinical Epidemiology Research Center (CERC), VA Connecticut Healthcare System, West Haven, CT, Yale University School of Medicine	New Haven, CT		CSP #572 Planning Committee; VA Clinical Epidemiology Research Center (CERC)
M	Antonelli						CSP #572 Planning Committee
M	de Asis						CSP #572 Planning Committee
MS	Bauer						CSP #572 Planning Committee
Mary	Brophy		MD MPH	Massachusetts Area Veterans Epidemiology, Research, and Information Center (MAVERIC), Jamaica Plain, MA, Boston University School of Medicine	Boston, MA		CSP #572 Planning Committee; CSP #572 Executive Committee; Million Veteran Program (MVP) Recruitment and Enrollment, Core Biorespository

Supplemental Online Content: Nonauthor Collaborators
*First name, last name, and suffix (if applicable) are required and will appear in PubMed.

***First Name and Middle Initial(s)**	***Last Name**	***Suffix (eg, Jr, III)**	Academic Degrees	Institution	Location (city, state/province, country)	Role or Contribution, eg, chair, principal investigator	Group (if more than 1 Group listed in the byline) and/or Subgroup (eg, Steering Committee)
John	Concato		MD	Yale University School of Medicine, New Haven, CT, Center for Drug Evaluation and Research, Food and Drug Administration	West Haven, CT		CSP #572 Planning Committee; CSP #572 Executive Committee; VA Clinical Epidemiology Rsearch Center (CERC) Director, Methodological Co-Principal Proponent; Million Veteran Program (MVP) Coordinating Center
F	Cunningham						CSP #572 Planning Committee
R	Freedman						CSP #572 Planning Committee
Michael	Gaziano		MD MPH	Massachusetts Area Veterans Epidemiology, Research, and Information Center (MAVERIC), Jamaica Plain, MA, Boston University School of Medicine	Boston, MA		CSP #572 Planning Committee; CSP #572 Executive Committee; Massachusetts Veterans Epidemiology Research and Information Center (MAVERIC) Director, Co-Principal Proponent; Million Veteran Program (MVP) Executive Committee (Co-Chair)
Theresa	Gleason		PhD	Office of Research and Development, Veterans Health Administration	Washington, D.C.		CSP #572 Planning Committee; VA Office of Research and Development, Director, Clinical Science Research and Development Service

Supplemental Online Content: Nonauthor Collaborators
*First name, last name, and suffix (if applicable) are required and will appear in PubMed.

***First Name and Middle Initial(s)**	***Last Name**	***Suffix (eg, Jr, III)**	Academic Degrees	Institution	Location (city, state/province, country)	Role or Contribution, eg, chair, principal investigator	Group (if more than 1 Group listed in the byline) and/or Subgroup (eg, Steering Committee)
Philip	Harvey		PhD	Bruce W. Carter Miami Veterans Affairs (VA) Medical Center, University of Miami Miller School of Medicine	Miami, FL	Study Co-Chair	CSP #572 Planning Committee; CSP #572 Executive Committee
Grant	Huang		MPH PhD	Office of Research and Development, Veterans Health Administration	Washington, D.C.		CSP #572 Planning Committee; VA Office of Research and Development, Director, Cooperative Studies Program; Million Veteran Program (MVP) Executive Committee
J	Kelsoe						CSP #572 Planning Committee
Thomas	Kosten		MD	Michael E. DeBakey VA Medical Center, Department of Psychiatry, Neuroscience, Pharmacology, and Immunology and Rheumatology, Baylor College of Medicine	Houston, TX		CSP #572 Planning Committee; CSP #572 Executive Committee
T	Lehner						CSP #572 Planning Committee
JB	Lohr						CSP #572 Planning Committee
SR	Marder						CSP #572 Planning Committee
P	Miller						CSP #572 Planning Committee

Supplemental Online Content: Nonauthor Collaborators
*First name, last name, and suffix (if applicable) are required and will appear in PubMed.

***First Name and Middle Initial(s)**	***Last Name**	***Suffix (eg, Jr, III)**	Academic Degrees	Institution	Location (city, state/province, country)	Role or Contribution, eg, chair, principal investigator	Group (if more than 1 Group listed in the byline) and/or Subgroup (eg, Steering Committee)
Timothy	O Leary		MD	Office of Research and Development, Veterans Health Administration	Washington, D.C.		CSP #572 Planning Committee; VA Office Research and Development, Chief Research and Development Officer Emeritus
T	Patterson						CSP #572 Planning Committee
P	Peduzzi						CSP #572 Planning Committee
Ronald	Przygodski		MD	Office of Research and Development, Veterans Health Administration	Washington, D.C.		CSP #572 Planning Committee; VA Office of Research and Development, Associate Director for Genomic Medicine and Acting Director of Biomedical Laboratory Research and Development Service
Larry	Siever			James J. Peters Veterans Affairs Medical Center, Icahn School of Medicine at Mount Sinai	Bronx, NY	Study Co-Chair	CSP #572 Planning Committee; CSP #572 Executive Committee
P	Sklar						CSP #572 Planning Committee; CSP #572 Executive Committee
S	Strakowski						CSP #572 Planning Committee

Supplemental Online Content: Nonauthor Collaborators
*First name, last name, and suffix (if applicable) are required and will appear in PubMed.

***First Name and Middle Initial(s)**	***Last Name**	***Suffix (eg, Jr, III)**	Academic Degrees	Institution	Location (city, state/province, country)	Role or Contribution, eg, chair, principal investigator	Group (if more than 1 Group listed in the byline) and/or Subgroup (eg, Steering Committee)
Hongyu	Zhao		PhD	Clinical Epidemiology Research Center (CERC), VA Connecticut Healthcare System, Yale University School of Medicine	New Haven, CT		CSP #572 Planning Committee; CSP #572 Executive Committee; MVP Science, Statistical Genetics
Ayman	Fanous		MD	VA New York Harbor Healthcare System, University of Arizona College of Medicine-Phoenix	Phoenix, AZ		CSP #572 Executive Committee; CSP #572 Site, Washington D.C.
W	Farwell						CSP #572 Executive Committee
A	Malhorta						CSP #572 Executive Committee
S	Mane						CSP #572 Executive Committee
P	Palacios						CSP #572 Executive Committee
Tim	Bigdeli		PhD	VA New York Harbor Healthcare System, Department of Psychiatry and Behavioral Sciences SUNY Downstate Health Sciences University	Brooklyn, NY		CSP #572 Executive Committee
M	Corsey			VA Healthcare System Bronx	Bronx, NY		CSP #572 Study Chairs' Office
L	Zaluda			VA Healthcare System Bronx	Bronx, NY		CSP #572 Study Chairs' Office
Juanita	Johnson		BSN	Bruce W. Carter Miami Veterans Affairs (VA) Medical Center	Miami, FL		CSP #572 Study Chairs' Office; CSP #572 Study Site, Miami
Melyssa	Sueiro		MS	Bruce W. Carter Miami Veterans Affairs (VA) Medical Center	Miami, FL		CSP #572 Study Chairs' Office

Supplemental Online Content: Nonauthor Collaborators
*First name, last name, and suffix (if applicable) are required and will appear in PubMed.

***First Name and Middle Initial(s)**	***Last Name**	***Suffix (eg, Jr, III)**	Academic Degrees	Institution	Location (city, state/province, country)	Role or Contribution, eg, chair, principal investigator	Group (if more than 1 Group listed in the byline) and/or Subgroup (eg, Steering Committee)
D	Cavaliere			Clinical Epidemiology Research Center (CERC), VA Connecticut Healthcare System	New Haven, CT		VA Clinical Epidemiology Research Center (CERC)
V	Jeanpaul			Clinical Epidemiology Research Center (CERC), VA Connecticut Healthcare System	New Haven, CT		VA Clinical Epidemiology Research Center (CERC)
Alysia	Maffucci		JD	Clinical Epidemiology Research Center (CERC), VA Connecticut Healthcare System	New Haven, CT		VA Clinical Epidemiology Research Center (CERC)
L	Mancini			Clinical Epidemiology Research Center (CERC), VA Connecticut Healthcare System	New Haven, CT		VA Clinical Epidemiology Research Center (CERC)
J	Deen						Massachusetts Veterans Epidemiology Research and Information Center (MAVERIC)
G	Muldoon						Massachusetts Veterans Epidemiology Research and Information Center (MAVERIC)
Stacey	Whitbourne		PhD		Boston, MA		Massachusetts Veterans Epidemiology Research and Information Center (MAVERIC); Million Veteran Program (MVP) Recruitment/Enrollment, Director/Deputy Director
J	Canive			Raymond G. Murphy VA Medical Center	Albuequerque, NM		CSP #572 Study Site, Albuquerque
L	Adamson			Raymond G. Murphy VA Medical Center	Albuequerque, NM		CSP #572 Study Site, Albuquerque
L	Calais			Raymond G. Murphy VA Medical Center	Albuequerque, NM		CSP #572 Study Site, Albuquerque

Supplemental Online Content: Nonauthor Collaborators
*First name, last name, and suffix (if applicable) are required and will appear in PubMed.

***First Name and Middle Initial(s)**	***Last Name**	***Suffix (eg, Jr, III)**	Academic Degrees	Institution	Location (city, state/province, country)	Role or Contribution, eg, chair, principal investigator	Group (if more than 1 Group listed in the byline) and/or Subgroup (eg, Steering Committee)
G	Fuldauer			Raymond G. Murphy VA Medical Center	Albuequerque, NM		CSP #572 Study Site, Albuquerque
R	Kushner			Raymond G. Murphy VA Medical Center	Albuequerque, NM		CSP #572 Study Site, Albuquerque
G	Toney			Raymond G. Murphy VA Medical Center	Albuequerque, NM		CSP #572 Study Site, Albuquerque
M	Lackey			Raymond G. Murphy VA Medical Center	Albuequerque, NM		CSP #572 Study Site, Albuquerque
A	Mank			Raymond G. Murphy VA Medical Center	Albuequerque, NM		CSP #572 Study Site, Albuquerque
N	Mahdavi			Raymond G. Murphy VA Medical Center	Albuequerque, NM		CSP #572 Study Site, Albuquerque
G	Villarreal			Raymond G. Murphy VA Medical Center	Albuequerque, NM		CSP #572 Study Site, Albuquerque
EC	Muly			Atlanta VA Medical Center	Atlanta, GA		CSP #572 Study Site, Atlanta
F	Amin			Atlanta VA Medical Center	Atlanta, GA		CSP #572 Study Site, Atlanta
M	Dent			Atlanta VA Medical Center	Atlanta, GA		CSP #572 Study Site, Atlanta
J	Wold			Atlanta VA Medical Center	Atlanta, GA		CSP #572 Study Site, Atla+A46:H59nta
B	Fischer			Baltimore VA Medical Center	Baltimore, MD		CSP #572 Study Site, Baltimore
A	Elliott			Baltimore VA Medical Center	Baltimore, MD		CSP #572 Study Site, Baltimore
C	Felix			Baltimore VA Medical Center	Baltimore, MD		CSP #572 Study Site, Baltimore
G	Gill			Baltimore VA Medical Center	Baltimore, MD		CSP #572 Study Site, Baltimore
PE	Parker			Birmingham VA Medical Center	Birmingham, AL		CSP #572 Site, Birmingham

Supplemental Online Content: Nonauthor Collaborators
*First name, last name, and suffix (if applicable) are required and will appear in PubMed.

***First Name and Middle Initial(s)**	***Last Name**	***Suffix (eg, Jr, III)**	Academic Degrees	Institution	Location (city, state/province, country)	Role or Contribution, eg, chair, principal investigator	Group (if more than 1 Group listed in the byline) and/or Subgroup (eg, Steering Committee)
C	Logan			Birmingham VA Medical Center	Birmingham, AL		CSP #572 Site, Birmingham
J	McAlpine			Birmingham VA Medical Center	Birmingham, AL		CSP #572 Site, Birmingham
LE	DeLisi			Brockton VA Medical Center	Brockton, MA		CSP #572 Site, Brockton
SG	Reece			Brockton VA Medical Center	Brockton, MA		CSP #572 Site, Brockton
MB	Hammer			Ralph H. Johnson VA Healthcare System	Charleston, SC		CSP #572 Site, Charleston
D	Agbor-Tabie			Ralph H. Johnson VA Healthcare System	Charleston, SC		CSP #572 Site, Charleston
W	Goodson			Ralph H. Johnson VA Healthcare System	Charleston, SC		CSP #572 Site, Charleston
M	Aslam			VA Cincinnati Healthcare System	Cincinnati, OH		CSP #572 Site, Cincinnati
M	Grainger			VA Cincinnati Healthcare System	Cincinnati, OH		CSP #572 Site, Cincinnati
Neil	Richtand			VA Cincinnati Healthcare System	Cincinnati, OH		CSP #572 Site, Cincinnati
Alexander	Rybalsky			VA Cincinnati Healthcare System	Cincinnati, OH		CSP #572 Site, Cincinnati
R	Al Jurdi			Michael E. DeBakey VA Medical Center	Houston, TX		CSP #572 Site, Houston
E	Boeckman			Michael E. DeBakey VA Medical Center	Houston, TX		CSP #572 Site, Houston
T	Natividad			Michael E. DeBakey VA Medical Center	Houston, TX		CSP #572 Site, Houston
D	Smith			Michael E. DeBakey VA Medical Center	Houston, TX		CSP #572 Site, Houston
M	Stewart			Michael E. DeBakey VA Medical Center	Houston, TX		CSP #572 Site, Houston

Supplemental Online Content: Nonauthor Collaborators
*First name, last name, and suffix (if applicable) are required and will appear in PubMed.

***First Name and Middle Initial(s)**	***Last Name**	***Suffix (eg, Jr, III)**	Academic Degrees	Institution	Location (city, state/province, country)	Role or Contribution, eg, chair, principal investigator	Group (if more than 1 Group listed in the byline) and/or Subgroup (eg, Steering Committee)
S	Torres			Michael E. DeBakey VA Medical Center	Houston, TX		CSP #572 Site, Houston
Z	Zhao			Michael E. DeBakey VA Medical Center	Houston, TX		CSP #572 Site, Houston
A	Mayeda			Richard L. Roudebush VA Medical Center	Indianapolis, IN		CSP #572 Site, Indianapolis
A	Green			Richard L. Roudebush VA Medical Center	Indianapolis, IN		CSP #572 Site, Indianapolis
J	Hofstetter			Richard L. Roudebush VA Medical Center	Indianapolis, IN		CSP #572 Site, Indianapolis
S	Ngombu			Richard L. Roudebush VA Medical Center	Indianapolis, IN		CSP #572 Site, Indianapolis
MK	Scott			Richard L. Roudebush VA Medical Center	Indianapolis, IN		CSP #572 Site, Indianapolis
A	Strasburger			Richard L. Roudebush VA Medical Center	Indianapolis, IN		CSP #572 Site, Indianapolis
J	Sumner			Richard L. Roudebush VA Medical Center	Indianapolis, IN		CSP #572 Site, Indianapolis
G	Paschall			John L. McClellan Memorial Veterans' Hospital	Little Rock, AR		CSP #572 Site, Little Rock
J	Mucciarelli			John L. McClellan Memorial Veterans' Hospital	Little Rock, AR		CSP #572 Site, Little Rock
R	Owen			John L. McClellan Memorial Veterans' Hospital	Little Rock, AR		CSP #572 Site, Little Rock
S	Theus			John L. McClellan Memorial Veterans' Hospital	Little Rock, AR		CSP #572 Site, Little Rock
D	Tompkins			John L. McClellan Memorial Veterans' Hospital	Little Rock, AR		CSP #572 Site, Little Rock
SG	Potkin			VA Long Beach Healthcare System	Long Beach, CA		CSP #572 Site, Long Beach
C	Reist			VA Long Beach Healthcare System	Long Beach, CA		CSP #572 Site, Long Beach

Supplemental Online Content: Nonauthor Collaborators
*First name, last name, and suffix (if applicable) are required and will appear in PubMed.

***First Name and Middle Initial(s)**	***Last Name**	***Suffix (eg, Jr, III)**	Academic Degrees	Institution	Location (city, state/province, country)	Role or Contribution, eg, chair, principal investigator	Group (if more than 1 Group listed in the byline) and/or Subgroup (eg, Steering Committee)
M	Novin			VA Long Beach Healthcare System	Long Beach, CA		CSP #572 Site, Long Beach
S	Khalaghizadeh			VA Long Beach Healthcare System	Long Beach, CA		CSP #572 Site, Long Beach
Richard	Douyon		MD	Bruce W. Carter Miami Veterans Affairs (VA) Medical Center	Miami, FL		CSP #572 Site, Miami
Nita	Kumar		MD	Bruce W. Carter Miami Veterans Affairs (VA) Medical Center	Miami, FL		CSP #572 Site, Miami
Becky	Martinez		MSN	Bruce W. Carter Miami Veterans Affairs (VA) Medical Center	Miami, FL		CSP #572 Site, Miami
SR	Sponheim			Minneapolis VA Healthcare System	Minneapolis, MN		CSP #572 Site, Minneapolois
TL	Bender			Minneapolis VA Healthcare System	Minneapolis, MN		CSP #572 Site, Minneapolois
HL	Lucas			Minneapolis VA Healthcare System	Minneapolis, MN		CSP #572 Site, Minneapolois
AM	Lyon			Minneapolis VA Healthcare System	Minneapolis, MN		CSP #572 Site, Minneapolois
MP	Marggraf			Minneapolis VA Healthcare System	Minneapolis, MN		CSP #572 Site, Minneapolois
LH	Sorensen			Minneapolis VA Healthcare System	Minneapolis, MN		CSP #572 Site, Minneapolois
CR	Surerus			Minneapolis VA Healthcare System	Minneapolis, MN		CSP #572 Site, Minneapolois
C	Sison			Montrose VA Medical Center	Montrose, NY		CSP #572 Site, Montrose
J	Amato			Montrose VA Medical Center	Montrose, NY		CSP #572 Site, Montrose
DR	Johnson			Montrose VA Medical Center	Montrose, NY		CSP #572 Site, Montrose
N	Pagan-Howard			Montrose VA Medical Center	Montrose, NY		CSP #572 Site, Montrose

Supplemental Online Content: Nonauthor Collaborators
*First name, last name, and suffix (if applicable) are required and will appear in PubMed.

***First Name and Middle Initial(s)**	***Last Name**	***Suffix (eg, Jr, III)**	Academic Degrees	Institution	Location (city, state/province, country)	Role or Contribution, eg, chair, principal investigator	Group (if more than 1 Group listed in the byline) and/or Subgroup (eg, Steering Committee)
LA	Adler			VA New York Harbor Healthcare System	New York, NY		CSP #572 Site, New York Harbor
S	Alerpin			VA New York Harbor Healthcare System	New York, NY		CSP #572 Site, New York Harbor
T	Leon			VA New York Harbor Healthcare System	New York, NY		CSP #572 Site, New York Harbor
KM	Mattocks			Northampton VA Medical Center	Leeds, MA		CSP #572 Site, Northampton
N	Araeva			Northampton VA Medical Center	Leeds, MA		CSP #572 Site, Northampton
JC	Sullivan			Northampton VA Medical Center	Leeds, MA		CSP #572 Site, Northampton
T	Suppes			VA Palo Alto Health Care System	Palo Alto, CA		CSP #572 Site, Palo Alto
K	Bratcher			VA Palo Alto Health Care System	Palo Alto, CA		CSP #572 Site, Palo Alto
L	Drag			VA Palo Alto Health Care System	Palo Alto, CA		CSP #572 Site, Palo Alto
EG	Fischer			VA Palo Alto Health Care System	Palo Alto, CA		CSP #572 Site, Palo Alto
L	Fujitani			VA Palo Alto Health Care System	Palo Alto, CA		CSP #572 Site, Palo Alto
S	Gill			VA Palo Alto Health Care System	Palo Alto, CA		CSP #572 Site, Palo Alto
D	Grimm			VA Palo Alto Health Care System	Palo Alto, CA		CSP #572 Site, Palo Alto
J	Hoblyn			VA Palo Alto Health Care System	Palo Alto, CA		CSP #572 Site, Palo Alto
T	Nguyen			VA Palo Alto Health Care System	Palo Alto, CA		CSP #572 Site, Palo Alto
E	Nikolaev			VA Palo Alto Health Care System	Palo Alto, CA		CSP #572 Site, Palo Alto

Supplemental Online Content: Nonauthor Collaborators
*First name, last name, and suffix (if applicable) are required and will appear in PubMed.

***First Name and Middle Initial(s)**	***Last Name**	***Suffix (eg, Jr, III)**	Academic Degrees	Institution	Location (city, state/province, country)	Role or Contribution, eg, chair, principal investigator	Group (if more than 1 Group listed in the byline) and/or Subgroup (eg, Steering Committee)
L	Shere			VA Palo Alto Health Care System	Palo Alto, CA		CSP #572 Site, Palo Alto
R	Relova			VA Palo Alto Health Care System	Palo Alto, CA		CSP #572 Site, Palo Alto
A	Vicencio			VA Palo Alto Health Care System	Palo Alto, CA		CSP #572 Site, Palo Alto
M	Yip			VA Palo Alto Health Care System	Palo Alto, CA		CSP #572 Site, Palo Alto
I	Hurford			Corporal Michael J. Crescenz VA Medical Center	Philadelphia, PA		CSP #572 Site, Philadelphia
S	Acheampong			Corporal Michael J. Crescenz VA Medical Center	Philadelphia, PA		CSP #572 Site, Philadelphia
G	Carfagno			Corporal Michael J. Crescenz VA Medical Center	Philadelphia, PA		CSP #572 Site, Philadelphia
GL	Haas			VA Pittsburgh Healthcare System	Pittsburgh, PA		CSP #572 Site, Pittsburgh
C	Appelt			VA Pittsburgh Healthcare System	Pittsburgh, PA		CSP #572 Site, Pittsburgh
E	Brown			VA Pittsburgh Healthcare System	Pittsburgh, PA		CSP #572 Site, Pittsburgh
B	Chakraborty			VA Pittsburgh Healthcare System	Pittsburgh, PA		CSP #572 Site, Pittsburgh
E	Kelly			VA Pittsburgh Healthcare System	Pittsburgh, PA		CSP #572 Site, Pittsburgh
G	Klima			VA Pittsburgh Healthcare System	Pittsburgh, PA		CSP #572 Site, Pittsburgh
S	Steinhauer			VA Pittsburgh Healthcare System	Pittsburgh, PA		CSP #572 Site, Pittsburgh
RA	Hurley			W.G. (Bill) Hefner VA Medical Center	Salisbury, NC		CSP #572 Site, Salisbury

Supplemental Online Content: Nonauthor Collaborators
*First name, last name, and suffix (if applicable) are required and will appear in PubMed.

***First Name and Middle Initial(s)**	***Last Name**	***Suffix (eg, Jr, III)**	Academic Degrees	Institution	Location (city, state/province, country)	Role or Contribution, eg, chair, principal investigator	Group (if more than 1 Group listed in the byline) and/or Subgroup (eg, Steering Committee)
R	Belle			W.G. (Bill) Hefner VA Medical Center	Salisbury, NC		CSP #572 Site, Salisbury
D	Eknoyan			W.G. (Bill) Hefner VA Medical Center	Salisbury, NC		CSP #572 Site, Salisbury
K	Johnson			W.G. (Bill) Hefner VA Medical Center	Salisbury, NC		CSP #572 Site, Salisbury
J	Lamotte			W.G. (Bill) Hefner VA Medical Center	Salisbury, NC		CSP #572 Site, Salisbury
E	Granholm			San Diego VA Medical Center	San Diego, CA		CSP #572 Site, San Diego
K	Bradshaw			San Diego VA Medical Center	San Diego, CA		CSP #572 Site, San Diego
J	Holden			San Diego VA Medical Center	San Diego, CA		CSP #572 Site, San Diego
RH	Jones			San Diego VA Medical Center	San Diego, CA		CSP #572 Site, San Diego
T	Le			San Diego VA Medical Center	San Diego, CA		CSP #572 Site, San Diego
IG	Molina			San Diego VA Medical Center	San Diego, CA		CSP #572 Site, San Diego
M	Peyton			San Diego VA Medical Center	San Diego, CA		CSP #572 Site, San Diego
I	Ruiz			San Diego VA Medical Center	San Diego, CA		CSP #572 Site, San Diego
L	Sally			San Diego VA Medical Center	San Diego, CA		CSP #572 Site, San Diego
A	Tapp			VA Medical Center- Tacoma	Tacoma, WA		CSP #572 Site, Tacoma
S	Devroy			VA Medical Center- Tacoma	Tacoma, WA		CSP #572 Site, Tacoma
V	Jain			VA Medical Center- Tacoma	Tacoma, WA		CSP #572 Site, Tacoma
N	Kilzieh			VA Medical Center- Tacoma	Tacoma, WA		CSP #572 Site, Tacoma
L	Maus			VA Medical Center- Tacoma	Tacoma, WA		CSP #572 Site, Tacoma
K	Miller			VA Medical Center- Tacoma	Tacoma, WA		CSP #572 Site, Tacoma
H	Pope			VA Medical Center- Tacoma	Tacoma, WA		CSP #572 Site, Tacoma
A	Wood			VA Medical Center- Tacoma	Tacoma, WA		CSP #572 Site, Tacoma
E	Meyer			Olin E. Teague Veterans' Medical Center (Temple)	Temple, TX		CSP #572 Site, Temple
P	Givens			Olin E. Teague Veterans' Medical Center (Temple)	Temple, TX		CSP #572 Site, Temple
PB	Hicks			Olin E. Teague Veterans' Medical Center (Temple)	Temple, TX		CSP #572 Site, Temple
S	Justice			Olin E. Teague Veterans' Medical Center (Temple)	Temple, TX		CSP #572 Site, Temple

Supplemental Online Content: Nonauthor Collaborators
*First name, last name, and suffix (if applicable) are required and will appear in PubMed.

***First Name and Middle Initial(s)**	***Last Name**	***Suffix (eg, Jr, III)**	Academic Degrees	Institution	Location (city, state/province, country)	Role or Contribution, eg, chair, principal investigator	Group (if more than 1 Group listed in the byline) and/or Subgroup (eg, Steering Committee)
K	McNair			Olin E. Teague Veterans' Medical Center (Temple)	Temple, TX		CSP #572 Site, Temple
JL	Pena			Olin E. Teague Veterans' Medical Center (Temple)	Temple, TX		CSP #572 Site, Temple
DF	Tharp			Olin E. Teague Veterans' Medical Center (Temple)	Temple, TX		CSP #572 Site, Temple
L	Davis			Tuscaloosa VA Medical Center	Tuscaloosa, AL		CSP #572 Site, Tuscaloosa
M	Ban			Tuscaloosa VA Medical Center	Tuscaloosa, AL		CSP #572 Site, Tuscaloosa
L	Cheatum			Tuscaloosa VA Medical Center	Tuscaloosa, AL		CSP #572 Site, Tuscaloosa
P	Darr			Tuscaloosa VA Medical Center	Tuscaloosa, AL		CSP #572 Site, Tuscaloosa
W	Grayson			Tuscaloosa VA Medical Center	Tuscaloosa, AL		CSP #572 Site, Tuscaloosa
J	Munford			Tuscaloosa VA Medical Center	Tuscaloosa, AL		CSP #572 Site, Tuscaloosa
D	Smith			Tuscaloosa VA Medical Center	Tuscaloosa, AL		CSP #572 Site, Tuscaloosa
B	Whitfield			Tuscaloosa VA Medical Center	Tuscaloosa, AL		CSP #572 Site, Tuscaloosa
E	Wilson			Tuscaloosa VA Medical Center	Tuscaloosa, AL		CSP #572 Site, Tuscaloosa
SE	Melnikoff			VA Washington DC Healthcare System	Washington, D.C.		CSP #572 Site, Washington, D.C.
BL	Schwartz			VA Washington DC Healthcare System	Washington, D.C.		CSP #572 Site, Washington, D.C.
MA	Tureson			VA Washington DC Healthcare System	Washington, D.C.		CSP #572 Site, Washington, D.C.
D	D Souza			West Haven VA Medical Center	West Haven, CT		CSP #572 Site, West Haven
K	Forselius			West Haven VA Medical Center	West Haven, CT		CSP #572 Site, West Haven
M	Ranganathan			West Haven VA Medical Center	West Haven, CT		CSP #572 Site, West Haven
L	Rispoli			West Haven VA Medical Center	West Haven, CT		CSP #572 Site, West Haven
M	Sather			New Mexico VA Healthcare System	Albuequerque, NM		CSP #572 CSP Coordinating Center (for monitoring), Director

Supplemental Online Content: Nonauthor Collaborators
*First name, last name, and suffix (if applicable) are required and will appear in PubMed.

***First Name and Middle Initial(s)**	***Last Name**	***Suffix (eg, Jr, III)**	Academic Degrees	Institution	Location (city, state/province, country)	Role or Contribution, eg, chair, principal investigator	Group (if more than 1 Group listed in the byline) and/or Subgroup (eg, Steering Committee)
C	Colling			New Mexico VA Healthcare System	Albuequerque, NM		CSP #572 CSP Coordinating Center (for monitoring)
C	Haakenson			New Mexico VA Healthcare System	Albuequerque, NM		CSP #572 CSP Coordinating Center (for monitoring)
D	Kruegar			New Mexico VA Healthcare System	Albuequerque, NM		CSP #572 CSP Coordinating Center (for monitoring)
Sumitra	Muralidhar		PhD	Office of Research and Development, Veterans Health Administration	Washington, D.C.		VA Office Research and Development, Senior Scientific Program Mnaager Genomic Medicine Program, Biomedical and Clinical R&D Services; Million Veteran Program (MVP) Executive Committee; MVP Program Office
Rachel	Ramoni		DMD ScD	Office of Research and Development, Veterans Health Administration	Washington, D.C.		Million Veteran Program (MVP) Executive Committee (Co-Chair)
Jim	Breeling		MD				Million Veteran Program (MVP) Executive Committee
Kyong-Mi	Chang		MD	Corporal Michael J. Crescenz VA Medical Center	Philadelphia, PA		Million Veteran Program (MVP) Executive Committee
Christopher	O Donnell		MD MPH	VA Boston Healthcare System	Boston, MA		Million Veteran Program (MVP) Executive Committee; MVP Science, Genomics

Supplemental Online Content: Nonauthor Collaborators
*First name, last name, and suffix (if applicable) are required and will appear in PubMed.

***First Name and Middle Initial(s)**	***Last Name**	***Suffix (eg, Jr, III)**	Academic Degrees	Institution	Location (city, state/province, country)	Role or Contribution, eg, chair, principal investigator	Group (if more than 1 Group listed in the byline) and/or Subgroup (eg, Steering Committee)
Philip	Tsao		PhD	VA Palo Alto Health Care System	Palo Alto, CA		Million Veteran Program (MVP) Executive Committee; MVP Coordinating Center, Genomics Coordinating Center; MVP Science, Genomics
Jennifer	Moser		PhD	Office of Research and Development, Veterans Health Administration	Washington, D.C.		Million Veteran Program (MVP) Office
Jessica	Brewer		MPH	VA Boston Healthcare System	Boston, MA		Million Veteran Program (MVP) Recruitment and Enrollment
Stuart	Warren		JD PharmD	New Mexico VA Healthcare System	Albuequerque, NM		Million Veteran Program (MVP) Recruitment and Enrollment, MVP Coordinating Center, Cooperative Studies Program Clinical Research Pharmacy Coordinating Center
Dean	Argyres		MS	New Mexico VA Healthcare System	Albuequerque, NM		Million Veteran Program (MVP) Recruitment and Enrollment, MVP Coordinating Center, Cooperative Studies Program Clinical Research Pharmacy Coordinating Center

Supplemental Online Content: Nonauthor Collaborators
*First name, last name, and suffix (if applicable) are required and will appear in PubMed.

***First Name and Middle Initial(s)**	***Last Name**	***Suffix (eg, Jr, III)**	Academic Degrees	Institution	Location (city, state/province, country)	Role or Contribution, eg, chair, principal investigator	Group (if more than 1 Group listed in the byline) and/or Subgroup (eg, Steering Committee)
Brady	Stevens		MS				Million Veteran Program (MVP) Recruitment and Enrollment, MVP Information Center- Canandaiggua
Donald	Humphries		PhD	VA Boston Healthcare System	Boston, MA		Million Veteran Program (MVP) Recruitment and Enrollment, Core Biorespository
Nhan	Do		MD	VA Boston Healthcare System	Boston, MA		Million Veteran Program (MVP) Recruitment and Enrollment, Informatics
Shahpoor	Shayan			VA Boston Healthcare System	Boston, MA		Million Veteran Program (MVP) Recruitment and Enrollment, Informatics
Xuan-Mai	Nguyen		PhD	VA Boston Healthcare System	Boston, MA		Million Veteran Program (MVP) Recruitment and Enrollment, Data Operations/Analytics
Saiju	Pyarajan		PhD	VA Boston Healthcare System	Boston, MA		Million Veteran Program (MVP) Science, Genomics; MVP Science, Data and Computational Sciences
Kelly	Cho		MPH PhD	VA Boston Healthcare System	Boston, MA		Million Veteran Program (MVP) Science, Phenomics
Elizabeth	Hauser		PhD	Duke University School of Medicine	Durham, NC		Million Veteran Program (MVP) Science, Statistical Genetics
Yan	Sun		PhD				Million Veteran Program (MVP) Science, Statistical Genetics

Supplemental Online Content: Nonauthor Collaborators
*First name, last name, and suffix (if applicable) are required and will appear in PubMed.

***First Name and Middle Initial(s)**	***Last Name**	***Suffix (eg, Jr, III)**	Academic Degrees	Institution	Location (city, state/province, country)	Role or Contribution, eg, chair, principal investigator	Group (if more than 1 Group listed in the byline) and/or Subgroup (eg, Steering Committee)
Peter	Wilson		MD	Atlanta VA Medical Center	Atlanta, GA	Local Site Investigator	Million Veteran Program (MVP)
Rachel	McArdle		PhD	Bay Pines VA Healthcare System	Bay Pines, FL	Local Site Investigator	Million Veteran Program (MVP)
Louis	Dellitalia		MD	Birmingham VA Medical Center	Birmingham, AL	Local Site Investigator	Million Veteran Program (MVP)
John	Harley		MD PhD	Cincinnati VA Healthcare System	Cincinnati, OH	Local Site Investigator	Million Veteran Program (MVP)
Jeffrey	Whittle		MD MPH	Clement J. Zablocki VA Medical Center	Milwaukee, WI	Local Site Investigator	Million Veteran Program (MVP)

Data Sharing Statement

Chang-Wolf. Performance of Polygenic Risk Scores for Primary Open-Angle Glaucoma in Populations of African Descent. *JAMA Ophthalmol*. Published November 14, 2024. doi:10.1001/jamaophthalmol.2024.4784

Data
Data available: No

Additional Information
Explanation for why data not available: The UKB data are available through the UK Biobank Access Management System https://www.ukbiobank.ac.uk/. The GWAS summary statistics generated in Gharahkhani et al. are available via the GWAS Catalog under study accession identifiers GCST90011766, GCST90011767, GCST90011768, GCST90011769, GCST90011770. GWAS summary statistics for the GGLAD dataset are available through the Journal of the American Medical Association (JAMA). The GWAS summary statistics from Han et al. and Craig et al. are available for research use at https://xikunhan.github.io/site/publication/. Individual-level data are not publicly available due to participant confidentiality. Upon publication of the full GWAS, the MVP summary statistics will be placed in dbGaP study accession number phs001672. Computer codes used to generate the results in this study are available upon reasonable request to the corresponding author.