

## Research article

# Exploring ethnic and racial differences in intraocular pressure and glaucoma: The Canadian Longitudinal Study on aging

Alyssa Grant<sup>a</sup>, Marie-Hélène Roy-Gagnon<sup>a</sup>, Joseph Bastasic<sup>a</sup>, Akshay Talekar<sup>a</sup>,  
Garfield Miller<sup>b,c</sup>, Gisele Li<sup>d</sup>, Ellen E. Freeman<sup>a,e,f,\*</sup>

<sup>a</sup> School of Epidemiology and Public Health, University of Ottawa, Ottawa, Canada

<sup>b</sup> Ottawa Eye Institute, The Ottawa Hospital, Ottawa, Canada

<sup>c</sup> Department of Ophthalmology, University of Ottawa, Ottawa, Canada

<sup>d</sup> Maisonneuve-Rosemont Hospital, Montreal, Canada

<sup>e</sup> Ottawa Hospital Research Institute, Canada

<sup>f</sup> Bruyère Research Institute, Ottawa, Canada

## A B S T R A C T

**Purpose:** To determine whether self-reported race/ethnicity is associated with intraocular pressure (IOP) and glaucoma and to explore whether any associations are due to social, behavioral, genetic, or health differences.

**Design:** Cross-sectional analysis of population-based data.

**Methods:** We used the Canadian Longitudinal Study on Aging Comprehensive Cohort, which consists of 30,097 adults aged 45–85 years. Race/ethnicity was self-reported. Corneal-compensated intraocular pressure (IOP) was measured in mmHg using the Reichert Ocular Response Analyzer. Participants were asked to report if they have ever had a diagnosis of glaucoma and whether they used eye care in the past year. A glaucoma polygenic risk score (PRS) was calculated. Logistic and linear regression models were used.

**Results:** Black individuals had higher mean IOP levels (beta coefficient ( $\beta$ ) = 1.46; 95% confidence interval [CI], 0.62, 2.30) while Chinese, Japanese and Korean ( $\beta$  = -1.00; 95% CI, -1.63, -0.38) and Southeast Asian and Filipino individuals ( $\beta$  = -1.56; 95% CI, -2.68, -0.43) had lower mean IOP levels as compared to White individuals after adjustment for sociodemographic, behavioral, genetic, and health-related variables. Black people were more likely to report glaucoma as compared to White people after adjustment (odds ratio [OR] = 2.43; 95% CI, 1.27, 4.64).

**Conclusion:** Racial and ethnic differences in IOP and glaucoma were identified. Adjusting for sociodemographic, behavioral, genetic, and health-related variables did not fully explain these differences. Longitudinal research is needed to further explore the reasons for these differences and to understand their relevance to disease pathogenesis and progression.

## 1. Introduction

Glaucoma, a leading cause of irreversible vision loss worldwide and estimated to affect 76 million people in 2020, consists of a group of optic neuropathies undergoing progressive degeneration of retinal ganglion cells [1–3]. Factors related to the development and progression of glaucoma have not been fully characterized but both genetic and environmental factors are important [1,4]. Currently, reduction of intraocular pressure (IOP) is the only method proven to treat glaucoma [5].

For reasons that we do not yet fully understand, type and frequency of glaucoma vary by ethnic background. People having European, African, and Latin American ancestry are much more likely to develop primary open-angle glaucoma (POAG) rather than

\* Corresponding author. 600 Peter Morand Crescent, Office 301H, School of Epidemiology and Public Health, University of Ottawa, Ottawa, Canada.

E-mail address: [efreeman@uottawa.ca](mailto:efreeman@uottawa.ca) (E.E. Freeman).

<https://doi.org/10.1016/j.heliyon.2024.e28611>

Received 17 August 2023; Received in revised form 20 March 2024; Accepted 21 March 2024

Available online 26 March 2024

2405-8440/© 2024 The Authors. Published by Elsevier Ltd. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

primary angle-closure glaucoma (PACG) while people of Asian ancestry may develop either POAG or PACG [3,6]. Furthermore, Black Americans have a higher prevalence of glaucoma than White Americans [7] with the prevalence in Hispanic Americans falling between the two [8]. Research has suggested that Black Americans may have an earlier age of onset of glaucoma and an increased progression to blindness [9,10], although other studies have reported similar visual field progression between Black and White Americans [11] and the Ocular Hypertension Treatment Study found that the association between Black race and the incidence of glaucoma disappeared when adjusting for other factors like central corneal thickness [12]. In addition, The Barbados Eye Study reported that Black participants had higher IOP than mixed race or White participants [13].

Prior studies have been limited in the number of ethnic groups that they have included. They have also failed to thoroughly investigate reasons for racial and ethnic differences in glaucoma and IOP. Using the baseline data from the Canadian Longitudinal Study on Aging (CLSA) that included multiple racial and ethnic groups of sufficient size, we investigated the associations between ethnicity, IOP, and glaucoma and assessed whether the associations were due to social, behavioral, genetic, health, or healthcare access factors.

## 2. Methods

### 2.1. Study population and design

A cross-sectional analysis was conducted using the first wave of data from the CLSA Comprehensive Cohort made up of 30,097 Canadian adults aged 45–85 years [14]. Stratified random sampling of provincial healthcare registration databases and random digit dialing of landline telephones was used to obtain the CLSA sample. The first wave of data was collected between 2012 and 2015 through in-home interviews and visits to data collection sites for physical examinations and biospecimen sample collections. These sites were located in cities across 7 provinces. Inclusion criteria were: participants had to be aged 45–85 years, living in the community, not cognitively impaired, and speak English or French. Exclusion criteria were: being a full-time member of the Canadian Armed Forces, living on a federal First Nations reserve or settlement, residing in a long-term care institution, or not a permanent resident or Canadian citizen.

### 2.2. Informed consent and ethics approval

All participants gave written informed consent. Research Ethics Board approval was acquired for all CLSA sites in July 2010. The University of Ottawa Office of Research Ethics and Integrity gave approval for the present analysis in October 2021 (H-12-18-2153).

### 2.3. Ocular data

Participants were asked to report any previous diagnosis of glaucoma by a doctor and whether they had visited an ophthalmologist or optometrist in the past year. Corneal-compensated IOP was evaluated using the Reichert Ocular Response Analyzer (Reichert Technologies, Depew, NY, USA). The IOP of the right and left eyes was averaged together for analysis. If one eye was missing IOP data, then the IOP value of the other eye was used. To estimate the pre-treatment IOP, the IOP of participants taking medications with a Drug Identification Number (DIN) of an IOP-lowering eye drop was divided by 0.7, which is the mean estimated treatment effect [15]. This approach has been used previously [16]. IOP values greater than 60 were treated as probable measurement errors and were excluded.

### 2.4. Race/ethnicity

Race/ethnicity was self-reported using an interviewer-administered questionnaire at baseline. In order to avoid small numbers, participants were grouped into 1 of 9 racial/ethnic groups including 1) White, 2) Black, 3) Chinese, Japanese and Korean, 4) Southeast Asian and Filipino, 5) South Asian, 6) Arab and West Asian, 7) Latin American, 8) Other, and 9) Mixed. People who reported being from more than one group were placed into the “Mixed” category.

### 2.5. Genetic data

Genome-wide genotyping of non-fasting blood samples from consenting participating were done using the Affymetrix Axiom array resulting in 794,409 single nucleotide polymorphisms (SNPs) from 26,622 participants [17]. Release 3 of the CLSA genomic data was used. Marker- and sample-based quality control checks were performed by the CLSA using standard procedures [17]. Marker-based checks were done for the examination of genotype consistency across genotyping batch, chromosomally defined sex, Hardy-Weinberg equilibrium, and discordance of genotyping across control replicates. Sample-based checks were done for the examination of relatedness, heterozygosity, and genotype missing values. 15 individuals were excluded with extreme values of heterozygosity and genotype missingness while 1666 individuals were excluded for relatedness. Release 3 also included genotype data imputed using the TOPMed reference panel at the University of Michigan Imputation Service. These imputed data contained 97,256 reference samples at 308,107,085 genetic markers [17].

A glaucoma polygenic risk score (PRS) was calculated for each CLSA participant having available genotype data that passed quality control checks. The PRS was previously developed by Craig et al. [18] using 2673 independent SNPs associated with glaucoma from their multitrait analysis of genome-wide association studies. Using genome build GRCh38/hg38, we had 2652 SNPs available in the

CLSA to calculate the PRS. Because there were so few missing SNPs (<1%), proxy SNPs were not chosen to replace the missing SNPs. The PRS was calculated for each CLSA participant with a weighted sum of the 2652 SNPs:  $\sum_{i=1}^{2652} \hat{\beta}_i \times \text{SNP}_i$ , where  $\hat{\beta}_i$  is the effect size of  $\text{SNP}_i$  on glaucoma from Craig et al. and  $\text{SNP}_i$  is the number of copies of the effect allele in an individual genotype or the expected number of copies of the effect alleles for imputed genotypes. We standardized the PRS to have a mean of 0 and standard deviation (SD) of 1.

Principal component analysis was performed on the CLSA genotype data and the top four principal components were clustered,

**Table 1**  
Average IOP by self-reported race/ethnicity, demographic, health, lifestyle, and genetic factors.

n = 25,398	IOP (mm Hg) Mean (SD)	P-value
<b>Race/ethnicity</b>		
White (n = 24,043)	16.1 (3.8)	ref
Black (n = 160)	17.2 (4.3)	0.004
Chinese, Japanese and Korean (n = 205)	15.0 (3.6)	<0.001
Southeast Asian and Filipino (n = 80)	14.6 (3.2)	0.007
South Asian (n = 209)	16.1 (3.6)	0.813
Arab and West Asian (n = 99)	15.6 (3.6)	0.306
Latin American (n = 82)	15.8 (4.0)	0.639
Other (n = 152)	16.4 (3.3)	0.312
Mixed (n = 364)	16.1 (3.8)	0.840
<b>Age group (years)</b>		
45-54 (n = 6452)	15.3 (2.7)	ref
55-64 (n = 8457)	16.2 (3.8)	<0.001
65-74 (n = 6202)	16.9 (4.9)	<0.001
75-85 (n = 4287)	17.1 (5.5)	<0.001
<b>Sex</b>		
Male (n = 12,792)	16.3 (4.0)	ref
Female (n = 12,606)	15.9 (3.7)	<0.001
<b>Education</b>		
University degree or certificate above (n = 5477)	16.0 (5.4)	ref
Bachelor's degree (n = 6014)	15.7 (5.0)	0.001
Less than Bachelor's degree (n = 13,864)	16.1 (3.3)	0.141
<b>Household income</b>		
≥\$100,000 (n = 8929)	15.7 (3.7)	ref
\$50,000- \$100,000 (n = 8422)	16.2 (4.0)	<0.001
\$20,000- \$50,000 (n = 5242)	16.3 (3.8)	<0.001
<\$20,000 (n = 1228)	16.1 (3.6)	0.074
Refused/Don't know (n = 1577)	16.0 (4.2)	0.036
<b>Smoking status</b>		
Current (n = 2145)	15.6 (3.2)	ref
Former (n = 11,154)	16.2 (3.9)	0.001
Never (n = 12,006)	16.0 (3.9)	<0.001
<b>Alcohol intake (grams/week)</b>		
T1 (n = 9979)	15.9 (3.7)	ref
T2 (n = 7739)	16.0 (3.9)	0.053
T3 (n = 7515)	16.3 (3.9)	<0.001
<b>Diabetes</b>		
None (n = 20,916)	15.9 (3.8)	ref
Type 1 (n = 136)	16.2 (4.4)	0.699
Type 2 (n = 2279)	16.8 (4.3)	<0.001
Suspect/neither type (n = 1809)	16.2 (3.7)	0.017
<b>High blood pressure</b>		
No (n = 11,348)	15.6 (3.7)	ref
Yes (n = 14,050)	16.5 (3.9)	<0.001
<b>BMI</b>		
Underweight (n = 169)	15.1 (3.8)	ref
Normal weight (n = 7406)	15.7 (3.9)	0.222
Overweight (n = 10,383)	16.1 (3.9)	<0.001
Obese (n = 7358)	16.3 (3.6)	<0.001
<b>Eye care utilization</b>		
No (n = 9987)	15.8 (3.4)	ref
Yes (n = 14,343)	16.3 (4.2)	<0.001
<b>PRS</b>		
Q1 (n = 6340)	15.0 (3.3)	ref
Q2 (n = 6352)	15.8 (3.6)	<0.001
Q3 (n = 6362)	16.4 (3.9)	<0.001
Q4 (n = 6344)	17.1 (4.1)	<0.001

\*The following variables had missing data: race/ethnicity (n = 4), education (n = 43), smoking (n = 93), alcohol (n = 165), diabetes (n = 258), BMI (n = 82), eye care utilization (n = 1068); ref = reference category.

yielding six clusters reflecting ancestry [17]. Each ancestry cluster was named by cross tabulating it with self-reported ethnicity and finding the dominant group.

## 2.6. Demographic, health, and lifestyle data

Age, sex, education and income were collected during the in-home visit via an interviewer-administered questionnaire. Participants had their height and weight measured using standardized procedures at data collection site visits. Body mass index (BMI) was calculated and categorized according to World Health Organization guidelines (underweight  $<18.5 \text{ kg/m}^2$ , normal weight  $18.5\text{--}24.9 \text{ kg/m}^2$ , overweight  $25.0\text{--}29.9 \text{ kg/m}^2$ , and obese  $\geq 30.0 \text{ kg/m}^2$ ) [19].

Participants were asked if they had a physician diagnosis of diabetes or high blood pressure. Also, blood pressure was measured 6 times using the BpTRU™ BPM200 Blood Pressure Monitor (Medaval, Dublin, Ireland). Readings 2 through 5 were averaged. Hypertension was defined if: 1) a participant reported a physician diagnosis of hypertension or 2) if the average systolic blood pressure was 130 mmHg or higher or 3) diastolic blood pressure was 80 mmHg or higher [20].

Participants were asked “Have you smoked at least 100 cigarettes in your life?” and “At the present time, do you smoke cigarettes daily, occasionally (at least once in last 30 days), or not at all (not in last 30 days)?” Answers to these questions were used to determine if a person was a current, former, or never smoker. A current smoker reported smoking at least 100 cigarettes and currently smokes daily or occasionally. A former smoker reported smoking at least 100 cigarettes in their lifetime but had not smoked in the last 30 days. Questions were asked about alcohol consumption frequency and type of alcohol consumed during the in-home visit. Total alcohol intake (grams/week) was obtained by multiplying the weekly number of portions of each alcohol type by 13.45 g (the total alcohol content of a standard portion size specified in the CLSA). Total alcohol intake was then divided into tertiles.

## 2.7. Statistical analysis

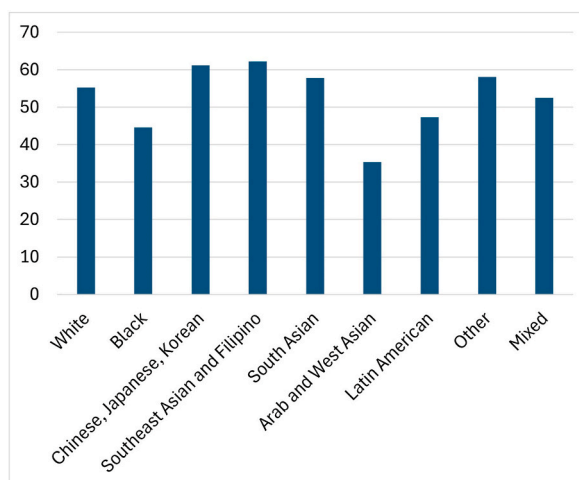
Our two primary outcomes were pre-treatment IOP and glaucoma. Mean IOP levels were examined by racial/ethnic, demographic, health, and behavioral factors. The proportion of participants that used eye care in the past 12 months and the distribution of the mean PRS were also examined by racial/ethnic group. Differences were tested by the linear and logistic regression. To adjust for potential confounding variables including age, sex, education, income, smoking, alcohol intake, diabetes, systemic hypertension, BMI, PRS, and province, linear regression was used for IOP while logistic regression was used for glaucoma. Given that race/ethnicity was self-reported, additional analyses were performed to examine PCA genetic ancestry clusters with IOP and glaucoma. Sensitivity analyses were done to examine current IOP instead of pre-treatment IOP and IOP in the left eye instead of mean iop. Sampling weights and strata variables were integrated into all analyses using the SVY commands in Stata SE 16 (StataCorp, College Station, TX, USA).

## 3. Results

### 3.1. Descriptive statistics

Our analysis sample consisted of 25,398 people (84% of the Comprehensive Cohort) who had complete genetic and IOP data with IOP measures within the accepted range (up to 60 mmHg). Those missing IOP and/or genetic data ( $n = 4699$ ) were very similar to those not missing data except they were older, more likely to be female, and drank less alcohol (Supplementary Table 1).

The mean IOP of participants by race/ethnicity, demographic, behavioral, health-related, and genetic factors is shown in Table 1.



**Fig. 1.** Percent of participants who had contact with an ophthalmologist or optometrist in past 12 months by self-reported racial/ethnic group.

Participants who were Black, older, had lower incomes, drank more alcohol, had type 2 diabetes or high blood pressure, had higher BMI, used eye care, and had higher glaucoma PRS scores had higher mean IOP levels ( $P < 0.05$ ). Chinese, Japanese, and Korean, Southeast Asian and Filipino participants, and women had lower IOP values ( $P < 0.05$ ).

The proportion of participants who had contact with an ophthalmologist or optometrist in the past 12 months by racial/ethnic group is presented in Fig. 1. Compared to White participants (55.3%), Arab and West Asian participants had the lowest proportion of eye care utilization (35.4%,  $P = 0.002$ ), followed by Black participants (44.6%,  $P = 0.043$ ). Southeast Asian and Filipino participants had the highest eye care utilization (62.2%) although it was not statistically significantly different from White participants ( $P = 0.420$ ).

The distribution of the standardized PRS by racial/ethnic group is shown in Table 2. A higher PRS may mean a higher genetic risk of glaucoma. The mean PRS differed significantly by racial/ethnic group. Black participants had the highest mean PRS (mean = 0.46,  $P < 0.001$ ) compared to White participants followed by Chinese, Japanese, and Korean people (mean = 0.37,  $P < 0.001$ ).

### 3.2. Regression models with self-reported ethnicity

In Table 3, linear regression was used to adjust the relationship between race/ethnicity and IOP for potentially confounding variables including age, sex, education, income, smoking, alcohol intake, BMI, diabetes, systemic hypertension, eye care utilization, and province. Model 1 adjusts for all variables except the PRS while Model 2 adjusts for all variables including the PRS. In Model 1, individuals of Black race had higher mean IOP levels (beta coefficient ( $\beta$ ) = 1.83; 95% confidence interval [CI], 1.00, 2.66) while Chinese, Japanese, and Korean ( $\beta = -0.70$ ; 95% CI, -1.32, -0.09) and Southeast Asian and Filipino individuals ( $\beta = -1.32$ ; 95% CI, -2.52, -0.12) had lower mean IOP levels as compared to White individuals after adjusting for sociodemographic, behavioral, and health-related variables. Adjusting for the PRS in Model 2 slightly attenuated the relationship between Black race and IOP ( $\beta = 1.46$ , 95% CI, 0.62, 2.30), although it remained statistically significant, while it increased the associations between Chinese, Japanese, and Korean ethnicity ( $\beta = -1.00$ , 95% CI, -1.63, -0.38) and Southeast Asian and Filipino ethnicity and IOP ( $\beta = -1.56$ , 95% CI, -2.68, -0.43).

The logistic regression results for glaucoma are shown in Table 4. In Model 1 of Table 4, individuals of Black race (odds ratio [OR] = 2.83; 95% CI, 1.47, 5.47) and Latin American ethnicity (OR = 2.64; 95% CI, 1.02, 6.82) were more likely to report glaucoma compared to White individuals after adjustment for demographic, behavioral, and health variables (Table 4). Further adjustment for the PRS (Model 2) somewhat attenuated the association between Black race and glaucoma (OR = 2.43, 95% CI 1.27, 4.64) although it remained statistically significant. Adjustment for the PRS attenuated the association between Latin American ethnicity and glaucoma (OR = 2.39, 95% CI 0.93, 6.14) such that it was no longer statistically significant.

### 3.3. Regression models with genetic markers of ancestry

Because self-reported race and ethnicity may not accurately reflect ancestry [21], especially in those with mixed ancestry, we conducted additional analyses instead using genetic markers of ancestry. Results were consistent with our main analyses using the self-report of race/ethnicity (Supplementary Table 2). Individuals of African descent had higher mean IOP ( $\beta = 2.06$ , 95% CI 1.27, 2.85), while individuals of East or Southeast Asian ancestry had lower mean IOP ( $\beta = -0.73$ , 95% CI -1.26, -0.21) as compared to individuals of European descent after covariate adjustment. As before, adjusting for the PRS somewhat attenuated the association between African ancestry and IOP while it strengthened the association between East or Southeast Asian ancestry and IOP.

Similarly, we examined the association between genetic ancestry and glaucoma (Supplementary Table 3). As with self-reported race/ethnicity, people of African descent were more likely to report glaucoma compared to individuals of European descent after adjustment (OR = 2.70, 95% CI 1.42, 5.13). Adjustment for the PRS somewhat reduced the strength of the association.

In contrast to our findings using self-reported ethnicity, people with genetic Latin American ancestry were not more likely to report glaucoma compared to those of European descent before (OR = 1.27, 95% CI 0.63, 2.55) or after PRS adjustment (OR = 1.21, 95% CI 0.62, 2.36). On the other hand, genetic Arab or West Asian ancestry was associated with glaucoma both before (OR = 1.55, 95% CI 1.03, 2.33) and after PRS adjustment (OR = 1.59, 95% CI 1.06, 2.38).

**Table 2**  
Mean standardized PRS by self-reported racial/ethnic group.

Race/ethnicity	PRS Mean (SD)	P-value
White	0.00 (1.00)	ref
Black	0.46 (0.70)	<0.001
Chinese, Japanese and Korean	0.37 (0.83)	<0.001
Southeast Asian and Filipino	0.23 (0.63)	0.029
South Asian	0.24 (0.91)	0.038
Arab and West Asian	-0.07 (0.87)	0.618
Latin American	0.28 (1.07)	0.103
Other	0.26 (0.95)	0.015
Mixed	-0.01 (0.86)	0.934

Ref = reference category.

**Table 3**  
Linear regression analyses of the associations of self-reported race/ethnicity with IOP.

	Model 1 <sup>a</sup> IOP n = 22,205 β (95% CI)	Model 2 <sup>b</sup> IOP n = 22,205 β (95% CI)
Race/ethnicity		
White	0.00	0.00
Black	1.83 (1.00, 2.66)	1.46 (0.62, 2.30)
Chinese, Japanese and Korean	-0.70 (-1.32, -0.09)	-1.00 (-1.63, -0.38)
Southeast Asian and Filipino	-1.32 (-2.52, -0.12)	-1.56 (-2.68, -0.43)
South Asian	0.56 (-0.09, 1.22)	0.37 (-0.34, 1.07)
Arab and West Asian	-0.02 (-0.88, 0.84)	0.08 (-0.71, 0.86)
Latin American	0.44 (-0.85, 1.73)	0.22 (-0.88, 1.33)
Other	0.57 (-0.13, 1.28)	0.34 (-0.38, 1.06)
Mixed	0.38 (-0.18, 0.94)	0.37 (-0.19, 0.93)
PRS	-	0.81 (0.74, 0.87)

<sup>a</sup> Adjusted for age, sex, education, income, smoking, alcohol intake, BMI, diabetes, high blood pressure, eye care utilization, and province.

<sup>b</sup> Adjusted for all covariates in model 1 and PRS.

**Table 4**  
Logistic regression analyses of the associations of self-reported race/ethnicity with glaucoma.

	Model 1 <sup>a</sup> Glaucoma n = 23,123 OR (95% CI)	Model 2 <sup>b</sup> Glaucoma n = 23,123 OR (95% CI)
Race/ethnicity		
White	1.00	1.00
Black	2.83 (1.47, 5.47)	2.43 (1.27, 4.64)
Chinese, Japanese and Korean	0.53 (0.15, 1.83)	0.46 (0.13, 1.62)
Southeast Asian and Filipino	2.63 (0.89, 7.78)	2.40 (0.82, 7.05)
South Asian	1.02 (0.49, 2.10)	0.98 (0.48, 1.98)
Arab and West Asian	1.63 (0.40, 6.59)	1.83 (0.46, 7.25)
Latin American	2.64 (1.02, 6.82)	2.39 (0.93, 6.14)
Other	2.20 (0.87, 5.54)	1.99 (0.78, 5.05)
Mixed	1.83 (0.74, 4.56)	1.91 (0.74, 4.90)
PRS	-	1.56 (1.42, 1.71)

<sup>a</sup> Adjusted for age, sex, education, income, smoking, alcohol intake, BMI, diabetes, high blood pressure, eye care utilization and province.

<sup>b</sup> Adjusted for all covariates in model 1 and PRS.

### 3.4. Sensitivity analyses

The results from the sensitivity analysis using current IOP measures were consistent with our main results (data not shown). Also, the results for IOP using data from only 1 eye are consistent with results using mean IOP (data not shown).

## 4. Discussion

We attempted to understand whether racial and ethnic differences in IOP and glaucoma are due to social, behavioral, genetic, health, or healthcare differences. We found that Black participants had higher mean IOP levels while Chinese, Japanese, and Korean, and Southeast Asian and Filipino participants had lower mean IOP levels as compared to White participants after adjustment. The PRS sometimes acted as a positive confounder (adjusting for it attenuated the association) and sometimes acted as a negative confounder (adjusting for it exaggerated the association). Adjustment for the PRS somewhat reduced the strength of the association with IOP among Black participants while it increased the strength of the association for Southeast Asian and Filipino individuals.

Furthermore, we found that individuals of Black race and Latin American ethnicity were more likely to report glaucoma as compared to White individuals, after adjusting for sociodemographic, behavioral, and health-related variables. Adjustment for the glaucoma PRS reduced the strength of the associations among Black and Latin American participants. Our results using the self-report of race and ethnicity were largely confirmed using measures of genetic ancestry. An exception was that only self-reported Latin American ancestry was associated with glaucoma before adjustment for the PRS while genetic Latin American ancestry was not. Further, genetic Arab or West Asian ancestry was associated with glaucoma while self-reported Arab or West Asian ancestry was not.

Documenting racial or ethnic differences in health without attempting to explain them is of limited value. Researchers need to consider the conceptual framework underlying their investigation into health disparities [22,23]. Too often, ethnic differences have been attributed to genetic causes without consideration of other social, behavioral, or health-related causes [24]. We identified several groups of factors that could potentially cause ethnic differences in IOP and glaucoma including social, behavioral, health, healthcare, and genetic factors. Despite adjusting for social factors like education and income, behavioral factors like alcohol consumption and smoking, health factors like diabetes and high blood pressure, and care factors like eye care in the last year, strong associations

between race/ethnicity and IOP and glaucoma remained. Further adjustment for the PRS somewhat attenuated our findings in Black participants while it somewhat strengthened our findings with IOP in Chinese, Japanese and Korean and Southeast Asian and Filipino individuals. Ultimately, we were not able to explain the racial and ethnic differences in IOP and glaucoma.

The CLSA is fairly unique in its large numbers of racial and ethnic groups allowing comparison of IOP between groups within the same study. Another very large study with multiple ethnic groups, the UK Biobank, also found that Black participants had higher IOP ( $\beta = 0.77$ , 95% CI 0.63, 0.90) and that Chinese participants had lower IOP ( $\beta = -0.74$ , 95% CI -1.10, -0.38) than White participants [25]. The Barbados Eye Study and South African Eye Study also found that Black participants had higher IOP than mixed race or White participants [13,26] and the Singapore Epidemiology of Eye Diseases Study reported that Chinese people had lower IOPs than Malay or Indian participants [27]. Our findings for glaucoma were also consistent with previous research. Several studies have previously reported that Black participants [7,28–30] and Latin American participants [8,31] were more likely to have glaucoma than White participants.

We did not find that a polygenic risk score, demographic, behavioral, or health-related factors explained the relationship between ethnicity and IOP/glaucoma. However, it's possible that other biological factors are related to ethnic differences. For example, although we had data on corneal-compensated IOP, we did not have data on other ocular biometric parameters. Researchers have previously identified structural and biometric parameters associated with POAG and its progression in African-Americans as compared to those of European descent including larger optic disc area, deeper maximum cup depth, and thinner corneas [32–35]. Further, African-American glaucoma patients were found in prior research to have higher levels of oxygen in the anterior chamber as compared to patients of European descent, which may contribute to increased oxidative stress, IOP, and cellular damage [36]. Studies have also shown African-American glaucoma patients to have significantly lower retrobulbar blood flow compared to patients of European descent [37,38].

Consistent with previous study results [39], Black and Latin American participants reported less contact with ophthalmologists and optometrists relative to White participants, which could put them at greater risk of developing glaucoma if they have untreated ocular hypertension. Arab and West Asian participants also were much less likely to have seen an ophthalmologist or optometrist in the last year. However, we did not find that adjustment for recent eye care use diluted racial and ethnic differences.

The main strength of this study is the use of a large population-based sample of multiple racial/ethnic groups and data on social, behavioral, health-related, and genetic factors. Several limitations must be noted. First, glaucoma status was based solely by self-report with no information available on severity or subtype. However, our findings with glaucoma are consistent with many other studies [7, 8,28–31]. Furthermore, data on retinal nerve fiber layer and macular thickness, structures implicated in glaucoma disease pathogenesis which have been previously found to vary according to race and ethnicity [40,41], were unavailable in the CLSA. Next, the use of a PRS constructed from European-derived variants, which may not replicate in non-European samples [42], may mean that we were not able to adequately adjust for the genetic risk of glaucoma. Therefore, we cannot rule out that the racial and ethnic differences in IOP and glaucoma are due to genetic differences. Also, although the CLSA had several racial and ethnic categories of participants, most of the categories were of limited size giving reduced statistical power to detect differences. Finally, beyond education and income, we did not have extensive data on social factors like experience with discrimination that could cause health disparities [22].

## 5. Conclusion

Racial and ethnic differences in IOP and glaucoma were identified. Adjusting for sociodemographic, behavioral, genetic, and health-related variables did not explain these differences. Longitudinal research is needed to further explore the reasons for these differences and to understand their relevance to disease pathogenesis and progression.

### Sponsor's role

Funding for the Canadian Longitudinal Study on Aging (CLSA) is provided by the Government of Canada through the Canadian Institutes of Health Research (CIHR) under grant reference: LSA 94473 and the Canada Foundation for Innovation, as well as the following provinces: Newfoundland, Nova Scotia, Quebec, Ontario, Manitoba, Alberta, and British Columbia. This research was funded by CIHR operating grant PJT-180615 to Drs Roy-Gagnon and Freeman. The funders had no role in the design, analysis, or the interpretation of results.

### Data availability statement

Data are available from the Canadian Longitudinal Study on Aging ([www.clsa-elcv.ca](http://www.clsa-elcv.ca)) for researchers who meet the criteria for access to de-identified CLSA data.

### Ethics declarations

This study was reviewed and approved by the University of Ottawa Office of Research and Integrity, with the approval number: H-12-18-2153.

All participants provided informed consent to participate in the study.

## Funding

This work was supported by the CIHR under Grants LSA 94,473 and PJT-180615.

## CRediT authorship contribution statement

**Alyssa Grant:** Writing – original draft, Formal analysis. **Marie-Hélène Roy-Gagnon:** Writing – review & editing, Supervision, Formal analysis. **Joseph Bastasic:** Writing – review & editing, Formal analysis. **Akshay Talekar:** Writing – review & editing, Formal analysis. **Garfield Miller:** Writing – review & editing, Conceptualization. **Gisele Li:** Writing – review & editing, Conceptualization. **Ellen E. Freeman:** Writing – review & editing, Supervision, Funding acquisition, Formal analysis, Conceptualization.

## Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: Marie-Helene Roy-Gagnon reports financial support was provided by Canadian Institutes of Health Research.

## Acknowledgments

This research was conducted using the CLSA Comprehensive Baseline Dataset version 6.0 under Application Number 180911. The CLSA is led by Drs. Parminder Raina, Christina Wolfson, and Susan Kirkland. The opinions expressed in this manuscript are the authors' own and do not reflect the views of the Canadian Longitudinal Study on Aging.

## Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.heliyon.2024.e28611>.

## References

- [1] R.N. Weinreb, T. Aung, F.A. Medeiros, The pathophysiology and treatment of glaucoma: a review, *JAMA* 311 (2014) 1901–1911, <https://doi.org/10.1001/jama.2014.3192>.
- [2] H. Quigley, A.T. Broman, The number of people with glaucoma worldwide in 2010 and 2020, *Br. J. Ophthalmol.* 90 (2006) 262–267, <https://doi.org/10.1136/bjo.2005.081224>.
- [3] Y.C. Tham, X. Li, T.Y. Wong, H.A. Quigley, T. Aung, C.Y. Cheng, Global prevalence of glaucoma and projections of glaucoma burden through 2040: a systematic review and meta-analysis, *Ophthalmology* 121 (11) (Nov 2014) 2081–2090, <https://doi.org/10.1016/j.ophtha.2014.05.013>.
- [4] R.W. Nickells, G.R. Howell, I. Soto, S.W.M. John, Under pressure: cellular and molecular responses during glaucoma, a common neurodegeneration with axonopathy, *Annu. Rev. Neurosci.* 35 (2012) 153–179, <https://doi.org/10.1146/annurev.neuro.051508.135728>.
- [5] M.V. Boland, A.M. Ervin, D.S. Friedman, et al., Comparative effectiveness of treatments for open-angle glaucoma: a systematic review for the U.S. Preventive Services Task Force, *Ann. Intern. Med.* 158 (4) (2013) 271–279, <https://doi.org/10.7326/0003-4819-158-4-201302190-00008>.
- [6] E.W. Chan, X. Li, Y.C. Tham, et al., Glaucoma in Asia: regional prevalence variations and future projections, *Br. J. Ophthalmol.* 100 (1) (Jan 2016) 78–85, <https://doi.org/10.1136/bjophthalmol-2014-306102>.
- [7] J.M. Tielsch, A. Sommer, J. Katz, R.M. Royall, H.A. Quigley, J. Javitt, Racial variations in the prevalence of primary open-angle glaucoma: the Baltimore eye survey, *JAMA, J. Am. Med. Assoc.* 266 (3) (1991) 369–374, <https://doi.org/10.1001/jama.1991.03470030069026>.
- [8] H.A. Quigley, S.K. West, J. Rodriguez, B. Munoz, R. Klein, R. Snyder, The prevalence of glaucoma in a population-based study of Hispanic subjects: proyecto VER, *Arch. Ophthalmol.* 119 (12) (2001) 1819–1826, <https://doi.org/10.1001/archophth.119.12.1819>.
- [9] The Advanced Glaucoma Intervention Study (AGIS), 3. Baseline characteristics of black and white patients, *Ophthalmology* 105 (7) (Jul 1998) 1137–1145, [https://doi.org/10.1016/s0161-6420\(98\)97012-9](https://doi.org/10.1016/s0161-6420(98)97012-9).
- [10] R. Wilson, T.M. Richardson, E. Hertzmark, W.M. Grant, Race as a risk factor for progressive glaucomatous damage, *Ann. Ophthalmol.* 17 (10) (1985) 653–659.
- [11] B. Melchior, I.A. Valenzuela, C.G. De Moraes, et al., Glaucomatous visual field progression in the african descent and glaucoma evaluation study (ADAGES): eleven years of follow-up, *Am. J. Ophthalmol.* 239 (Jul 2022) 122–129, <https://doi.org/10.1016/j.ajo.2022.02.003>.
- [12] M.O. Gordon, J.A. Beiser, J.D. Brandt, et al., The Ocular Hypertension Treatment Study: baseline factors that predict the onset of primary open-angle glaucoma, *Arch. Ophthalmol.* 120 (6) (Jun 2002) 714–720, <https://doi.org/10.1001/archophth.120.6.714> ; discussion 829–30.
- [13] M.C. Leske, A.M.S. Connell, S.Y. Wu, L. Hyman, A.P. Schachat, Distribution of intraocular pressure: the Barbados eye study, *Arch. Ophthalmol.* 115 (8) (1997) 1051–1057, <https://doi.org/10.1001/archophth.1997.01100160221012>.
- [14] P. Raina, C. Wolfson, S. Kirkland, et al., Cohort profile: the Canadian longitudinal study on aging (CLSA), *Int. J. Epidemiol.* 48 (2019) 1752–1753J, <https://doi.org/10.1093/ije/dyz173>.
- [15] R. Van Der Valk, C.A.B. Webers, J.S.A.G. Schouten, M.P. Zeegers, F. Hendrikse, M.H. Prins, Intraocular pressure-lowering effects of all commonly used glaucoma drugs: a Meta-analysis of randomized clinical trials, *Ophthalmology* 112 (7) (2005) 1177–1185, <https://doi.org/10.1016/j.ophtha.2005.01.042>.
- [16] A.P. Khawaja, J.N. Cooke Bailey, N.J. Wareham, et al., Genome-wide analyses identify 68 new loci associated with intraocular pressure and improve risk prediction for primary open-angle glaucoma, *Nat. Genet.* 50 (6) (Jun 2018) 778–782, <https://doi.org/10.1038/s41588-018-0126-8>.
- [17] V. Forgetta, R. Li, C. Darmond-Zwaig, et al., Cohort profile: genomic data for 26 622 individuals from the Canadian Longitudinal Study on Aging (CLSA), *BMJ Open* 12 (3) (Mar 10 2022) e059021, <https://doi.org/10.1136/bmjopen-2021-059021>.
- [18] J.E. Craig, X. Han, A. Qassim, et al., Multitrait analysis of glaucoma identifies new risk loci and enables polygenic prediction of disease susceptibility and progression, *Nat. Genet.* 52 (2) (2020), <https://doi.org/10.1038/s41588-019-0556-y>.
- [19] WHO, A healthy lifestyle - WHO recommendations. <https://www.euro.who.int/en/health-topics/disease-prevention/nutrition/a-healthy-lifestyle/body-mass-index-bmi>.
- [20] P.K. Whelton, R.M. Carey, W.S. Aronow, et al., ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/PCNA guideline for the prevention, detection, evaluation, and management of high blood pressure in adults: executive summary: a report of the American college of cardiology/American Heart Association task, 2018, *Hypertension* 71 (6) (2017) 1269–1324, <https://doi.org/10.1161/HYP.000000000000066>.



- [21] T.B. Mersha, T. Abebe, Self-reported race/ethnicity in the age of genomic research: its potential impact on understanding health disparities, *Hum. Genom.* 9 (1) (2015) 1, <https://doi.org/10.1186/s40246-014-0023-x>.
- [22] A.V. Diez Roux, Conceptual approaches to the study of health disparities, *Annu. Rev. Publ. Health* 33 (2012) 41–58, <https://doi.org/10.1146/annurev-publhealth-031811-124534>.
- [23] L.N. Borrell, J.R. Elhawary, E. Fuentes-Afflick, et al., Race and genetic ancestry in medicine — a time for reckoning with racism, *N. Engl. J. Med.* 384 (5) (2021) 474–480, <https://doi.org/10.1056/nejms2029562>.
- [24] M.T. Cabrera, A. Chen, It's time we reform our perspectives on race and glaucoma, *Transl Vis Sci Technol* 11 (9) (2022) 22, <https://doi.org/10.1167/tvst.11.9.22>.
- [25] M.P. Chan, C.M. Grossi, A.P. Khawaja, et al., Associations with intraocular pressure in a large Cohort: results from the UK Biobank, *Ophthalmology* 123 (4) (Apr 2016) 771–782, <https://doi.org/10.1016/j.ophtha.2015.11.031>.
- [26] S.O. Baboolal, D.P. Smit, South African Eye Study (SAES): ethnic differences in central corneal thickness and intraocular pressure, *Eye* 32 (4) (Apr 2018) 749–756, <https://doi.org/10.1038/eye.2017.291>.
- [27] J. Chua, Y.C. Tham, J. Liao, et al., Ethnic differences of intraocular pressure and central corneal thickness: the Singapore Epidemiology of Eye Diseases study, *Ophthalmology* 121 (10) (Oct 2014) 2013–2022, <https://doi.org/10.1016/j.ophtha.2014.04.041>.
- [28] A. Sommer, J.M. Tielsch, J. Katz, et al., Racial differences in the cause-specific prevalence of blindness in East Baltimore, *N. Engl. J. Med.* 325 (20) (1991) 1412–1417, <https://doi.org/10.1056/nejm199111143252004>.
- [29] M.C. Leske, A.M. Connell, A.P. Schachat, L. Hyman, The Barbados Eye Study. Prevalence of open angle glaucoma, *Arch. Ophthalmol.* 112 (6) (Jun 1994) 821–829, <https://doi.org/10.1001/archoph.1994.01090180121046>.
- [30] D.S. Friedman, H.D. Jampel, B. Munoz, S.K. West, The prevalence of open-angle glaucoma among blacks and whites 73 years and older: the Salisbury Eye Evaluation Glaucoma Study, *Arch. Ophthalmol.* 124 (11) (Nov 2006) 1625–1630, <https://doi.org/10.1001/archoph.124.11.1625>.
- [31] R. Varma, M. Ying-Lai, B.A. Francis, et al., Prevalence of open-angle glaucoma and ocular hypertension in Latinos: the Los Angeles Latino Eye Study, *Ophthalmology* 111 (8) (2004) 1439–1448, <https://doi.org/10.1016/j.ophtha.2004.01.025>.
- [32] C.A. Girkin, G. McGwin, A. Xie, J. Deleon-Ortega, Differences in optic disc topography between black and white normal subjects, *Ophthalmology* 112 (1) (2005) 33–39, <https://doi.org/10.1016/j.ophtha.2004.07.029>.
- [33] R.Y. Lee, G. Huang, T.C. Porco, Y.C. Chen, M. He, S.C. Lin, Differences in iris thickness among African Americans, caucasian Americans, hispanic Americans, Chinese Americans, and Filipino-Americans, *J. Glaucoma* 22 (9) (2013) 673–678, <https://doi.org/10.1097/IJG.0b013e318264ba68>.
- [34] L. Racette, M.R. Wilson, L.M. Zangwill, R.N. Weinreb, P.A. Sample, Primary open-angle glaucoma in blacks: a review, *Surv. Ophthalmol.* 48 (3) (May-Jun 2003) 295–313, [https://doi.org/10.1016/s0039-6257\(03\)00028-6](https://doi.org/10.1016/s0039-6257(03)00028-6).
- [35] F.A. La Rosa, R.L. Gross, S. Orengo-Nania, Central corneal thickness of Caucasians and African Americans in glaucomatous and nonglaucomatous populations, *Arch. Ophthalmol.* 119 (1) (Jan 2001) 23–27.
- [36] C.J. Siegfried, Y.B. Shui, N.M. Holekamp, F. Bai, D.C. Beebe, Racial differences in ocular oxidative metabolism: implications for ocular disease, *Arch. Ophthalmol.* 129 (7) (2011) 849–854, <https://doi.org/10.1001/archophthalmol.2011.169>.
- [37] B. Siesky, A. Harris, J. Carr, et al., Reductions in retrolubar and retinal capillary blood flow strongly correlate with changes in optic nerve head and retinal morphology over 4 years in open-angle glaucoma patients of African descent compared with patients of European descent, *J. Glaucoma* 25 (9) (2016) 750–757, <https://doi.org/10.1097/IJG.0000000000000520>.
- [38] B. Siesky, A. Harris, L. Racette, et al., Differences in ocular blood flow in glaucoma between patients of African and European descent, *J. Glaucoma* 24 (2) (2015) 117–121, <https://doi.org/10.1097/IJG.0b013e31829d9bb0>.
- [39] Y. Murakami, B.W. Lee, M. Duncan, et al., Racial and ethnic disparities in adherence to glaucoma follow-up visits in a county hospital population, *Arch. Ophthalmol.* 129 (7) (2011) 872–878, <https://doi.org/10.1001/archophthalmol.2011.163>.
- [40] L.Y.C. Poon, H. Antar, E. Tsikata, et al., Effects of age, race, and ethnicity on the optic nerve and peripapillary region using spectral-domain OCT 3d volume scans, *Translational Vision Science and Technology* 7 (6) (2018), <https://doi.org/10.1167/tvst.7.6.12>.
- [41] K.H. Wong, Y.C. Tham, D.Q. Nguyen, et al., Racial differences and determinants of macular thickness profiles in multiethnic Asian population: the Singapore Epidemiology of Eye Diseases Study, *Br. J. Ophthalmol.* 103 (7) (2019) 894–899, <https://doi.org/10.1136/bjophthalmol-2018-312447>.
- [42] G. Sirugo, S.M. Williams, S.A. Tishkoff, The missing diversity in human genetic studies, *Cell* 177 (1) (2019) 26–31, <https://doi.org/10.1016/j.cell.2019.02.048>.