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Publication Date

2022-07-01

DOI

10.1016/j.ajo.2022.02.003

Peer reviewed

HHS Public Access

Author manuscript

Am J Ophthalmol. Author manuscript; available in PMC 2023 July 01.

Published in final edited form as:

Am J Ophthalmol. 2022 July ; 239: 122–129. doi:10.1016/j.ajo.2022.02.003.

Glaucomatous Visual Field Progression in the African Descent and Glaucoma Evaluation Study (ADAGES): Eleven Years of Follow-up

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Abstract

Purpose: To compare the rates of visual field (VF) progression between individuals of Black and White race and to investigate whether treatment effects may help explain differences previously reported between racial groups.

Design: Multicenter prospective observational cohort study.

Methods: Participants with open angle glaucoma excluding those that had < 5 VF tests and < 2 years of follow-up, or any disease that could affect the optic nerve or the VF. The VF mean deviation (MD) slopes over time (dB/year) were calculated with linear regression models.

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We investigated socioeconomic (SE) variables, rates of glaucoma surgery, medications, treated intraocular pressure (IOP), and central corneal thickness (CCT).

Setting: Tertiary care glaucoma clinics.

Results: A total of 516 eyes were included with a mean (95% CI) follow-up time of 11.0 (10.5 to 11.5) years and 15.0 (14.1 to 15.8) visits. Participants of Black race were significantly younger (59.7 vs 66.9 years old, P < 0.01). The mean CCT and SE variables were similar between Black and White groups (P = 0.21 and P = 0.56, respectively), as were treatment with topical medications (P = 0.90) and the rate of VF MD change (−0.24 [−0.31 to −0.17] dB/year vs −0.32 [−0.36 to −0.27], P= 0.11), despite higher treated mean IOP (14.9 [14.5 to 15.4] vs 14.0 [13.6 to 14.4] mmHg, P=0.03) and fewer trabeculectomies (29.5% vs 50.0%, p < 0.01) in the Black race group.

Conclusions: Rates of VF progression were similar despite higher treated IOP in the Black race group. Mitigation of health access disparities in this study may have equalized previously reported different rates of VF progression between racial groups.

Table of contents statement

It has been postulated that socioeconomic differences between individuals of Black and White race may affect glaucoma progression. This article aimed to compare the rates of visual field progression between them and to investigate whether treatment effects may help explain differences previously reported between racial groups. Mitigation of health access disparities in this study may have equalized previously reported different rates of visual field progression between racial groups.

INTRODUCTION

Glaucoma is a leading cause of irreversible blindness among individuals over the age of 40 years and has a global prevalence of approximately 3.5%.[1,2] In the United States, the prevalence of primary-open angle glaucoma (POAG) is higher among individuals of Black race, who also have higher risk for becoming visually impaired from glaucoma when compared to White race individuals.[3–6] Several factors, including genetics, differences in central corneal thickness (CCT), and medical comorbidities, have been posited to explain some of this discrepancy in prevalence and severity of disease between the two races.[7,8] Several determinants of health, including socioeconomic status and access to healthcare, have also been suggested to explain these disparities.

Differences between Black and White race participants with glaucoma extend beyond clinical evaluation.[9] Recent studies have shown that glaucomatous Black race participants have higher test-retest variability on standard automated perimetry (SAP) compared to White race participants, which could lead to delay in detection of progression and late intervention in the former group.[10] Additionally, the impact of medical and surgical intervention on visual field (VF) progression between racial groups remains to be fully elucidated. There is scant data comparing rates of VF progression between racial groups when accounting for treated intraocular pressure (IOP) in long, prospective studies.

The purpose of this study is to compare the rates of VF progression between treated Black and White race glaucoma participants and to investigate whether different treatment modalities help explain racial differences in VF progression in a prospective, longitudinal study.

METHODS

The multi-site African Descent and Glaucoma Evaluation Study (ADAGES) collaboration (clinicaltrials.gov Identifier: NCT00221923) is a clinical trial that includes the Hamilton Glaucoma Center at the Department of Ophthalmology, University of California-San Diego (UCSD) (data coordinating center), the Edward S. Harkness Eye Institute at Columbia University Irving Medical Center, and the Department of Ophthalmology at University of Alabama-Birmingham (UAB). The institutional review boards at all sites approved the study methodology, which adheres to the tenets of the Declaration of Helsinki and to the Health Insurance Portability and Accountability Act. All participants gave written informed consent.

ADAGES is an observational, prospective cohort study that aimed to identify factors accounting for differences in glaucoma onset and rate of progression between Black and White race participants with confirmed or suspected glaucoma. Treatment targets were determined at each physician's discretion and did not follow any specific guidelines.

The ocular testing performed in ADAGES has been described elsewhere.[7] In brief, participants were asked to identify their race by self-report using the National Eye Institute inclusion/enrollment system describing ethnicity and race (http://orwh.od.nih.gov/pubs/outreach.pdf [pages 120–121]). They underwent a comprehensive ophthalmologic examination, including annual review of medical history, best-corrected visual acuity (BCVA), slit-lamp biomicroscopy, IOP measurement by Goldmann tonometry, dilated funduscopic examination, pachymetry, simultaneous stereoscopic optic disc photography, and SAP testing with the 24–2 SITA (Swedish Interactive Threshold Algorithm) Standard (Carl Zeiss Meditec, Inc., Dublin, CA, USA). Visual fields (VF) were repeated every 6 months and optic disc photographs were performed every 12 months.

ADAGES followed a rigid manual of procedures for all tests performed and was uniform across sites and participants. All technicians had to be certified by the reading center and had follow up communication to ensure quality throughout the study. The reading center also reviewed all test results in real-time and ensured tests were repeated if did not meet pre-defined quality criteria.

Inclusion and Exclusion Criteria

In the present report, only individuals with manifest POAG (open anterior chamber angle, stereophotograph based glaucomatous optic neuropathy as determined by two masked graders, and the presence of at least 3 consecutive abnormal SAP visual field tests) were included. An abnormal 24–2 VF required a pattern standard deviation with $P < 5\%$ or a Glaucoma Hemifield Test result "outside normal limits".[7]

All participants had a BCVA ≥ 20/40, and a refractive error < 5.0 diopters sphere and < 3.0 diopters cylinder at baseline. For the original ADAGES study, at least one high-quality stereophotograph and one reliable (< 33% false positives, false negatives and fixation losses) SAP Humphrey 24–2 field test result at baseline were required. Both eyes were included, except in cases where only one eye met the study criteria. Diabetic participants without evidence of retinopathy were included. In this study, races other than Black and White were excluded (27 participants).

Participants were not included if they had any ocular or systemic disease that could affect the optic nerve or the VF results. All ADAGES participants were experienced with perimetry and learning effects were ruled out by the University of California San Diego Visual Field Assessment Center (VisFACT). In this report, unreliable VF tests (considered as false positives > 15% and fixation losses > 20%) and individuals with fewer than 5 visits or less than 2 years of follow-up were not included. Participants with missing data (e.g. about medications and surgeries) were excluded (84 participants).

Statistical Analyses

Mean deviation (MD) slopes over time (dB/year) were calculated with linear regression models. The residuals, defined as the difference between the best fitted value and the observed measurement of the VF MD, were obtained for each data point of each eye over time. Visual field variability was defined as the standard deviation (SD) of these residuals as previously described.[11–13] The VF variability was compared between 1) eyes of Black and White race participants and 2) different glaucoma severity stages, defined based upon the baseline MD: mild (better than −5 dB), moderate (−5 to −10 dB) and severe (worse than −10 dB).

Given the study by Gracitelli et al,[10] which showed that a delay in detecting progression among Black compared to White race individuals may result from a higher VF variability in the former group, we performed a similar analysis aimed at matching for the specificity to detect progression taking into account false-positive rates due to variability. Computer simulations were performed based upon the real sample baseline mean MD and residuals derived from linear regression of the MD over time as recently described.[10,13] After simulating 10,000 stable eyes (slopes = 0.0 dB/year), the “noise” from the distribution of residuals was added to each time point of the fitted (predicted) regression lines. The residuals from simulated eyes of Black and White race individuals were derived from their own real-world distributions. The p-value that resulted in <5% of the sample with a significant negative slope was used to define the alpha-level that would match the groups for specificity. For more details, refer to Wu et al.[14]

Central corneal thickness (CCT) and the following treated IOP parameters were assessed: baseline (at study entry), peak (highest measurement during follow-up), mean (average of all follow up visits), and fluctuation (standard deviation (SD) of all visits). Note that baseline IOP was not the IOP before treatment beginning (untreated IOP), as the informations before study entry were not available for all participants. Multivariable analysis was performed with linear mixed effect models adjusting for between-eye correlations and an unstructured variance-covariance matrix adjusting for the relationship between baseline severity and rate

of progression. All IOP measurements were obtained with Goldmann tonometry during regular office hours (8am to 5pm).

Glaucoma surgeries (trabeculectomy, glaucoma long-tube implants, minimally invasive glaucoma surgery, laser trabeculoplasty, and glaucoma surgery revisions) were also assessed for each eye, as well as classes of glaucoma medications (beta adrenergic antagonists [beta-blocker], alpha-agonists, carbonic anhydrase inhibitors, prostaglandin analogues, miotics, and rho-kinase inhibitors) at each visit. The frequencies of surgeries and medications in each group were evaluated. Because glaucoma participants often undergo multiple medication changes during follow-up, we devised a method to account not only for the classes of medication in use, but also for what proportion of the follow-up visits each medication was being used. To achieve that purpose for each eye, we calculated how many visits each medication was being used as well how many medications were being used at each visit. Based on the total number of visits between the first and last VF, we then calculated the proportion of visits with the medication in use (visits in use/total visits). For instance, if an eye underwent 10 visits, 2 of which on a beta-blocker and 3 on beta-blocker + prostaglandin analogue, that eye was thus on a beta-blocker 50% of the time, 30% on a prostaglandin analogue, and 30% on 2 glaucoma medications simultaneously (beta-blocker combined with prostaglandin analogue). Medication use was based on self-report at the time of each visit.

Statistical analyses were performed using STATA (version 14; StataCorp LP, College Station, TX). We performed a sample size calculation for a linear mixed effects model with the following parameters: follow-up for 11 years, tests performed twice a year, average slope of −0.30 dB/yr, standard deviation of the slope of 0.3, average intercept of −6 dB, standard deviation of the intercept of 1.5, standard deviation of the residuals of 1.4, and effect size difference of 0.1 dB/yr. The estimated minimum sample size required was 300 for an 80% statistical power and 5% alpha level.

RESULTS

A total of 7,729 24–2 VF tests from 516 glaucomatous eyes (156 from Black and 360 from White race individuals) of 346 participants (108 Black and 238 White) were included. The mean (95% CI) follow-up time was 11.0 (10.5 to 11.5) years spanning 15.0 (14.1 to 15.8) visits. Participants were 55.2% women, with a similar distribution between the groups of Black and White race participants. The demographic and characteristics by race are shown in Table 1. The socioeconomic (SE) variables were collected by self-reported questionnaire for all participants (however, some of them declined to answer some questions), including education level, marital status, income, people in household, if other language was spoken and if they had health insurance. There were no SE significant difference between Black and White race participants ($p = 0.56$). MD variability was significantly higher in eyes of Black race individuals compared to White (Figure 1). However, despite the higher variability, the mean rate of MD change in the Black race participants group (−0.24; −0.31 to −0.17 dB/yr) was similar to the White group (−0.32 dB/yr; −0.36 to −0.27; p=0.11). The treated mean IOP in White was lower than Black race participants, although no significant differences were seen in baseline IOP, peak IOP, and IOP fluctuation between the two groups.

Computer simulations showed no significant difference in the proportion of progressing eyes detected in the real-world sample based on conventional statistical significance (i.e.: negative MD slope at $p < 0.05$) or matching for specificity both among eyes of Black (44% vs 44%, respectively) as well as White participants (47% vs 43%, respectively).

There were significantly more glaucoma surgeries performed in eyes of White race individuals (76.3%) compared to Black race (60.2%; $p< 0.01$). In particular, the number of trabeculectomies was greater among eyes of White race participants (50.0% versus 29.5%; $p< 0.01$). The rates of glaucoma surgeries are summarized in Table 2.

Given the differences in rates of glaucoma surgery between groups, we investigated whether these procedures were performed closer to the beginning versus end of the period when the VF tests were done. This is relevant because surgeries performed closer to beginning of follow-up may have had greater impact on the rates of VF change after the procedure when compared to those performed towards end of follow-up (which were more likely performed to slow/halt past rapid progression). We found that trabeculectomies were more likely to be performed later during follow-up among eyes of Black than White race participants (Black race mean: 1,317 days from baseline test, 95% CI: 727 to 1,907 vs White race mean: 469 days from baseline test, 95% CI: 100 to 838, $p=0.03$).

Medication use during the study period is summarized in Table 3. Black race were on alpha-agonists during more visits than White race participants group. Also, Black race participants were more likely to be on 2 glaucoma medications simultaneously when compared to White participants. None of the participants/eyes in any group was on 3 or more glaucoma medications during the study period.

The results of the multivariable model are shown in Table 4. After adjusting for other risk factors, each mmHg higher mean IOP resulted in a more rapid MD rate of change 0.02 dB/yr (more negative slope). Note that Black race participants group remained non-significantly associated with more rapid VF rates of change even after adjusting for other known risk factors. The inclusion of socioeconomic variables did not affect the results. After adjusting for socioeconomic variables, there remained no significant difference in rates of progression between groups. Before adjusting for socioeconomic variables, the P value of the interaction Race × Time (which compares the slopes between the two groups) was $P= 0.41$ (Table 4). After adjusting, it remained non significant at $P=0.48$.

DISCUSSION

In this prospective, longitudinal study we compared the rates of visual field progression between Black and White race participants with manifest glaucoma followed for a mean of 11 years. We found that the rates of progression were similar between groups. Of note, Black race participants had higher treated mean IOP, were less likely to undergo trabeculectomy, and were on a similar topical regimen as White race participants. These findings suggest that despite a more aggressive disease at presentation among Black race individuals (defined by baseline MD), treatment in this study was able to equalize the rates of progressive functional loss between racial groups.

In addition to treatment, other potential reasons for similar rates of progression between groups were addressed. Gracitelli et al[10] previously showed with computer simulations that the increased VF variability among individuals of Black race can delay progression detection and result in seemingly slower rates of MD change. For a scenario with baseline MD of −10 dB and rate of change of −0.5 dB/y, detection of progression in Black race participants was delayed by 3.1 years in a model of annual testing. A previous study[15] showed that, on average, the VF variability must be reduced by approximately 20% for a clinical improvement in detection of significant VF change. Increased variability may also result in false positives (false progression), leading the participants to unnecessary additional treatments. However, the delayed detection of progression can result in irreversible visual loss and loss of follow-up which can ensue from mistakenly assuming the patient is stable. Our simulation models confirmed their findings but, after matching for specificity, increased variability alone was not sufficient to explain the differences between groups.

Previous studies found higher prevalence and more rapid progression among Black race when compared to White race individuals,[16–18] and thus higher risk of visual impairment from glaucoma in Black race. However, during study follow-up when all participants were treated and monitored closely, such potential faster rates were not observed and both groups progressed at statistically similar rates. The apparent discrepancy between these findings and the existing literature can be in part explained by the fact that previous population based studies (Barbados Eye Study, Baltimore Eye Survey, and Salisbury Eye Evaluation),[5,16,19–22] which showed faster rates of visual field MD change in Black race participants, analyzed data in an environment where socioeconomic disparities and differences in access to treatment may have adversely affected individuals of Black race.[23,24] Among these social disparities, Black race participants encounter more barriers to health care (e.g., lack of insurance, transportation, and access to medications)[25,26] which can negatively affect health outcomes. These socioeconomic disparities between individuals of Black and White race[10] could be partly responsible for the worse baseline MD at younger age among Black race participants at study entry. These disparities may have been mitigated, at least in part, in a research setting like ADAGES, in which similar health care access was ensured per protocol, as well as close monitoring, visit reminders, free medications, and support for transportation. Also, in the sample of this study, there were no significant socioeconomic differences between Black and White race participants.

Our results are consistent with the Ocular Hypertension Treatment Study (OHTS), in which Black race was a significant risk factor for conversion to glaucoma in the univariate analysis, but when other risk factors were included in a multivariable model (e.g, CCT, cup-to-disc ratio, IOP, and visual field PSD), race was no longer statistically associated with the development of a POAG endpoint.[27,28] Similar findings were reported in the ADAGES population with suspected glaucoma.[8]

This was an observational cohort study with treatment decisions at physician discretion, which can be a potential confounder. Trabeculectomies were done later during follow-up among eyes of Black race participants; in other words, White race participants were operated sooner. Participants of Black race tended to progress more slowly based upon visual fields, which may help explain why surgery tended to be performed later in this

group. In addition, IOP fluctuation was higher (although not significantly so) among White race group, likely due to IOP changes caused by their higher number of trabeculectomy procedures.[29] However, the comparison between IOP parameters and their effects on rates of VF progression should ideally be evaluated in a prospective randomized clinical trial in which participants are subjected to the same treatment targets.

With regard to topical medications, there were overall no significant differences between the two groups with the exception of Black race participants being more likely to be on alpha-agonists and on two different classes of medications simultaneously. Individuals of White race were more likely to be on miotics although the numbers in each group were small.

Our study has limitations. First, we did not adjust tonometric measurements for CCT, despite CCT being a potential confounder to IOP measurement[30]. However, Brandt et al[31] have shown that adjusting IOP for CCT does not improve prediction models for POAG. Yet, our multivariable model adjusted for the effect of CCT as a confounder. Second, we employed a global summary statistic (MD) as a parameter for visual field progression which may miss local visual field changes. However, Wu et al[13] have compared pointwise event-based (GPA) and global trend-based analysis (MD) and found that they had similar power to detect glaucoma progression when matched for specificity. The use of MD also can simulate a higher rate of progression when media opacities are due to aging (e.g. cataract), which could explain in part a trend for more rapid progression among White race participants, given that they were older than Black race participants in this sample. However, we observed significantly more cataract surgery among individuals of White race. This probably benefited the White race group from an MD slope standpoint, as the slopes become less negative after surgery. Third, IOP values were based upon office-hour measurements, which do not take into account the IOP fluctuation that occurs around the clock and which could play a role in glaucoma progression.[32] However, in clinical practice and clinical trials, office-hour measurements remain the most common method to assess IOP and its relationship to rates of VF change. Fourth, the group of Black race participants was significantly younger than the White race group. However, the multivariable analysis was adjusted for age to minimize this effect. Finally, medication adherence was based on self-report, which is known to have significant limitations.

The age difference has significant clinical implications, though. Given that the rate of visual field progression was similar between Black and White race participants, but Black race individuals were younger at baseline, a larger proportion of Black race glaucoma participants may develop visual impairment in their lifetime compared to White race participants. This possibility, combined with the higher variability of visual field results (delaying the detection of progression)[10] may help explain the higher rates of visual impairment seen in the real world and reported in previous population based studies.

In summary, in this prospective, longitudinal study, treated Black and White racea participants with manifest glaucoma progressed at similar rates. Our results suggest that once barriers to healthcare are mitigated (e.g.: improved access to medication, more frequent visual field testing, improved adherence to office visits through phone calls), the differences

in rates of progression seen outside the research setting in the real-world can be overcome and yield improved health outcomes in glaucoma management.

ACKNOWLEDGEMENTS

a) Funding/Support: National Eye Institute Grants U10EY14267, EY08208, EY11008, EY019869, EY13959, 1EY027510, EY025253) - Bethesda, MD; Eyesight Foundation of Alabama - Birmingham, AL; Alcon Laboratories Inc. - Fort Worth, TX; Allergan Inc. - Dublin, Ireland; Pfizer Inc. - New York, NY; Merck Inc. - Rahway, NJ; Santen Inc. - Osaka, Japan; unrestricted departmental grant from Research to Prevent Blindness, New York, NY (Department of Ophthalmology, Columbia University Medical Center and Department of Ophthalmology, University of California San Diego), Edith C. Blum Foundation, New York, NY, Bernard Schwartz Travel Grant from the American Glaucoma Society, San Francisco, CA; Coordenação de Aperfeiçoamento de Pessoal de Nível Superior (CAPES), Brasília, DF, Brazil

b) Financial Disclosures: BM, IAV, CGDM, JSP, CAG, and GAC have no financial disclosures. RNW receives grants from Bausch & Lomb, consulting fees from Allergan and Nicox, and equipment, materials, gifts, or other services from Heidelberg Engineering, Topcon, Optovue, Centervue. JML receives support from Carl Zeiss Meditech, Inc. (Instrument Support), Heidelberg Engineering, GmbH (Instrument support). No conflicting relationship exists for any author.

c) Other Acknowledgements: None.

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HIGHLIGHTS

- Previous studies have reported worse visual field outcomes in glaucoma patients of Black race compared to White race
- We found that visual field progression differences between Black and White race patients with glaucoma are similar when access to care and care delivery are also similar in a research setting

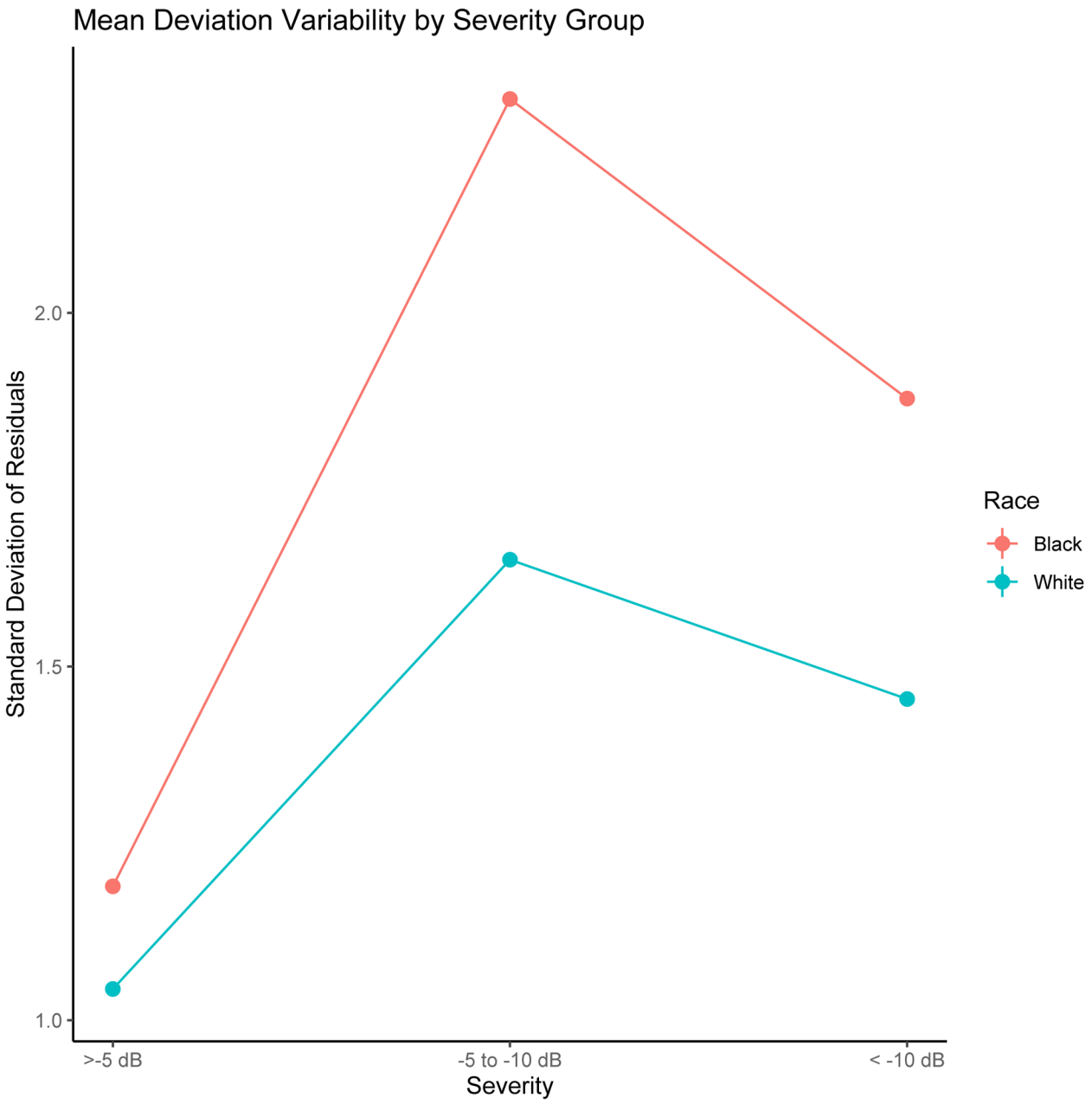

Figure 1.
Standard deviation of mean deviation (MD) residual over predicted MD (dB) for Black and White race participants.

Table 1.

Demographic, Visual Field and Intraocular Pressure Characteristics by Race

	Black Race Participants		White Race Participants		P
	Mean	**95% CI**	**Mean**	**95% CI**	
Patients					
Age at Baseline (years)	59.7	57.2 to 62.2	66.9	65.7 to 68.2	<0.01
Sex (% female)	55.6	-	55.0	-	1.00
Follow up (years)	11.7	11.0 to 12.5	10.6	9.9 to 11.2	0.03
Number of Visits	14.8	13.6 to 16.0	14.9	13.9 to 16.0	0.89
Central Corneal Thickness (μm)	530.1	523.9 to 536.3	537.3	533.0 to 541.7	0.20
Visual Field Parameters					
Baseline Mean Deviation (dB)	6.40	−7.61 to 5.19	−5.29	−5.86 to 4.72	0.06
Rates of MD change (dB/year)	−0.24	−0.31 to − 0.17	−0.32	−0.36 to − 0.27	0.11
Variability (residual variance - SD)	1.62	−4.65 to 4.77	1.29	−1.59 to 2.51	<0.01
Treated IOP (mmHg)					
Baseline	17.0	16.2 to 17.7	16.2	15.7 to 16.8	0.23
Mean	14.9	14.5 to 15.4	14.0	13.6 to 14.4	0.03
Peak	21.2	20.2 to 22.2	20.3	19.6 to 21.1	0.34
Fluctuation (SD)	3.1	2.8 to 3.4	3.3	3.1 to 3.5	0.18
Socioeconomic Variables					0.56

	No.	**(%)**	**Not reported****	**No.**	**(%)**	**Not Reported****	
Insurance (yes)	93	(86.1%)	11.1%	175	(73.5%)	25.2%	0.01
Education level (at least high school degree)	90	(83.3%)	7.4%	177	(74.4%)	22.7%	0.07
Income (>$25,000/year)	50	(46.3%)	38.9%	122	(51.3%)	42.0%	0.42
People in household (<3)	64	(59.2%)	21.3%	129	(54.2%)	42.4%	0.41
Marital Status (married)	41	(37.9%)	10.2%	103	(43.3%)	25.2%	0.41
Other language spoken (yes)	8	(7.4%)	10.2%	26	(10.9%)	25.6%	0.34

95% CI = 95% Confidence Interval; dB = decibel; SD = Standard Deviation; MD = Mean Deviation

Linear mixed effects models adjusting for inter-eye correlations

* Variance test

** Declined, not reported or missing data

Table 2.

Glaucoma and Cataract Surgeries by Race

Surgeries	Black Race Participants		White Race Participants		P
	Total	Percentage (95% CI)	Total	Percentage (95% CI)	
Trabeculectomy	46	29.5 (22.4 to 37.3)	180	50.0 (44.7 to 55.2)	<0.001
Trabeculoplasty	78	50.0 (41.9 to 58.1)	219	60.8 (55.5 to 65.9)	0.022
Surgery revision	16	10.2 (5.9 t 16.1)	30	8.3 (5.6 to 11.6)	0.481
Glaucoma Valve Implant	5	3.2 (1.0 to 7.3)	7	1.9 (0.7 to 3.9)	0.383
MIGS	3	1.9 (0.4 to 5.5)	9	2.5 (1.1 to 4.6)	0.690
Any Glaucoma Surgery	94	60.2 (52.1 to 67.9)	275	76.3 (71.6 to 80.6)	<0.001
Cataract Extraction	81	51.9 (43.7 to 59.9)	264	73.3 (68.4 to 77.8)	<0.001

*95% CI = 95% Confidence Interval; *MIGS = Minimally Invasive Glaucoma

Table 3.

Proportion of Time During Follow-up Using Glaucoma Topical Medications by Race

Medications	Black Race Participants		White Race Participants		P
	Mean (%)	95% CI	Mean (%)	95% CI	
Beta-blockers	22.7	19.5 to 25.9	25.1	22.8 to 27.3	0.533
Alpha Agonists	13.5	11.0 to 15.9	8.4	7.1 to 9.8	<0.001
Carbonic Anhydrase Inhibitor (topical)	17.7	14.8 to 20.6	16.8	15.0 to 18.7	0.959
Prostaglandin Analogues	40.4	36.9 to 43.9	39.0	36.3 to 41.6	0.432
Rho-kinase Inhibitors	0.1	0.0 to 0.2	0.1	0 to 0.1	0.450
Miotics	0.1	0.0 to 0.3	1.6	0.9 to 2.2	0.007
Any Glaucoma Medication	81.2	76.9 to 85.5	81.6	79.0 to 84.1	0.905
One Glaucoma medication	67.5	63.1 to 71.9	72.0	69.3 to 74.7	0.155
Two Glaucoma Medication	13.7	11.0 to 16.5	9.5	79.2 to 11.1	0.008

Table 4.

Univariable and Multivariable Analysis of The Effects of Race, Corneal Thickness, Intraocular Pressure and Age on The Rate of Visual Field Mean Deviation Change

	Univariable Analysis			Multivariable Analysis		
	Coef.	**95% CI**	**P**	**Coef.**	**95% CI**	**P**
Race (reference: Black race)	1.41	0.07 to 2.75	0.039	1.69	0.36 to 3.02	0.013
Race # Time (reference: Black race)	−0.06	−0.14 to −0.02	0.181	−0.03	−0.13 to 0.05	0.412
CCT (per 40 microns)	1.27	0.68 to 1.85	< 0.001	0.77	0.20 to 1.34	0.007
CCT # Time (per 40 microns)	0.00	−0.03 to 0.04	0.717	0.02	0.01 to 0.06	0.246
Mean IOP (per mmHg)	0.62	0.47 to 0.77	< 0.001	0.60	0.45 to 0.76	<0.001
Mean IOP # Time (per mmHg)	−0.02	−0.03 to −0.01	< 0.001	−0.02	−0.03 to −0.01	<0.001
Baseline Age (per decade)	0.18	−0.37 to 0.73	0.521	−0.2	−0.33 to 0.75	0.450
Baseline Age #Time (per decade)	−0.06	−0.10 to −0.03	< 0.001	−0.06	−0.10 to −0.03	<0.001

CCT = Central Corneal Thickness; IOP = Intraocular Pressure

#denotes the interaction term that tests for differences in slopes in the mixed effects model