# Identifying Risk Factors for Blindness From Glaucoma at First Presentation to a Tertiary Clinic



### ALYSSA SHI, SAMUEL I. BERCHUCK, ALESSANDRO A. JAMMAL, GEETIKA SINGH, SYDNEY HUNT, KIMBERLY ROCHE, SAYAN MUKHERJEE, AND FELIPE A. MEDEIROS

• PURPOSE: Glaucoma is the leading cause of irreversible blindness, a crippling disability resulting in higher risks of chronic health conditions. To better understand disparities in blindness risk, we identified risk factors of blindness on first presentation to a glaucoma clinic using a large clinical database.

• DESIGN: Retrospective cross-sectional study.

• METHODS: We used electronic health records of glaucoma patients from the Duke Ophthalmic Registry. *International Classification of Diseases* codes were used to identify glaucoma and exclude concurrent diseases. Blindness classification was based on the definition of legal blindness. Risk factors included gender, race, marital status, age, intraocular pressure, diabetes history, income level, and education. Odds ratios (ORs) and 95% CIs were calculated for risk factors using univariable and multivariable logistic regression.

• RESULTS: Our cohort consisted of 3753 patients, with 192 (5%) blind on first presentation. In univariable models, African American / Black race (OR 2.48, 95% CI 1.83-3.36), single marital status (1.74, 95% CI 1.25-2.44), prior diabetes diagnosis (2.23, 95% CI 1.52-3.27), and higher intraocular pressure (1.29 per 1 SD higher, 95% CI 1.13-1.46) were associated with increased risk of presenting blind, whereas higher annual income (0.75, 95% CI 0.65-0.86) and education (0.77, 95% CI 0.69-0.85) were associated with lower risk. These associations remained significant and in the same

direction in a multivariable model apart from income, which became insignificant.

• CONCLUSIONS: Using a large real-world clinical database, we identified risk factors associated with presentation with blindness among glaucoma patients. Our results highlight disparities in health care outcomes and indicate the importance of targeted education to reduce disparities in blindness. (Am J Ophthalmol 2023;250: 130–137. © 2023 Elsevier Inc. All rights reserved.)

G LAUCOMA IS A PROGRESSIVE EYE DISEASE THAT affects the optic nerve and can result in irreversible blindness.<sup>1</sup> Worldwide, it is estimated that 76 million people have glaucoma between the ages of 40 and 80 years.<sup>2</sup> Of these, approximately 11.6 million people are bilaterally blind from glaucoma, making it the leading cause of irreversible blindness.<sup>3</sup>

Blindness is a crippling disability that hinders a person's ability to perform routine daily tasks and is associated with feelings of loneliness, loss of independence, social isolation, and depression.<sup>4,9</sup> Additionally, visual impairment is associated with a greater risk of mortality, unintentional injury, and chronic conditions.<sup>10-12</sup> Furthermore, according to Medical Expenditure Panel Survey data from 1996 to 2002, those who are blind or visually impaired experience higher medical care costs, greater amounts of informal health care, and decreased quality of life.<sup>13</sup>

Because of these negative effects, early diagnosis and treatment of glaucoma are important to track the progression of the disease and reduce the risk of blindness. However, early glaucoma diagnosis can be difficult as the condition often remains asymptomatic until late stages.<sup>14</sup> As a result, groups that do not have an accurate comprehension of the disease or that have less access to health care may be less likely to seek care and therefore more likely to have vision loss due to glaucoma. For example, a study of 152 glaucoma patients at a San Francisco hospital found that Black and Latino patients were more likely than White patients (odds ratios: 7.16 and 4.77, respectively) to be inconsistent with follow-up appointments, potentially because of lack of understanding about the consequences of glaucoma.<sup>15</sup> Additionally, studies have found that blindness due to glaucoma

AJO.com Supplemental Material available at AJO.com.

Meeting Presentation: This work was presented as a talk at the 2021 Virtual ARVO Annual Meeting.

Accepted for publication February 2, 2023.

From Duke University (A.S., S.H.), Durham, North Carolina, USA; Department of Statistical Science, Duke University (S.I.B., S.M.), Durham, North Carolina, USA; Duke Eye Center and Department of Ophthalmology, Duke University (A.A.J., F.A.M.), Durham, North Carolina, USA; PathAI (G.S.), Boston, Massachusetts, USA; Tempus Labs, Inc (K.R.), Durham, North Carolina, USA; Departments of Mathematics, Computer Science, Biostatistics & Bioinformatics, Duke University (S.M.), Durham, North Carolina, USA; Center for Scalable Data Analytics and Artificial Intelligence, Universität Leipzig (S.M.), Leipzig, Germany; Max Planck Institute for Mathematics in the Sciences (S.M.), Leipzig, Germany.

Inquiries to Felipe A. Medeiros, Visual Performance Laboratory, Duke Eye Center and Department of Ophthalmology, Duke University, Durham, North Carolina, USA; e-mail: felipe.medeiros@duke.edu

Descargado para Eilyn Mora Corrales (emorac17@gmail.com) en National Library of Health and Social Security de ClinicalKey.es por Elsevier en junio 16, 2023. Para uso personal exclusivamente. No se permiten otros usos sin autorización. Copyright ©2023. Elsevier Inc. Todos los derechos reservados.

is 6 to 8 times more likely for Black Americans compared to White.  $^{16}$ 

Little work has been done on risk factors for presenting to a care center already blind as opposed to over the course of treatment. This is important, as studies have shown that progression to blindness is relatively uncommon in developed countries if a patient is being treated. As such, it is likely that the largest decrease in blindness from glaucoma can be achieved from public education and targeted public screening to reduce the risk of presenting for treatment already blind.<sup>17</sup> Therefore, risk factors for presenting blind may provide insight on populations that seek care "too late" and may require targeted public screening and education on glaucoma. A previous case-control study found no statistical difference in presentation with blindness between Black and White patients; however, the study had only 37 Black case-control pairs and 19 White case-control pairs, did not examine other demographic variables, and did not primarily focus on blindness at presentation.<sup>18</sup>

In this study, we investigated a large cohort of glaucoma patients to identify risk factors of blindness on first presentation. The study cohort was curated from electronic health records (EHRs) from the Duke Ophthalmic Registry (DOR), leveraging clinical and demographic data available on first presentation to highlight disparities in blindness risk before clinical care at a tertiary care center. We hypothesized that disadvantaged sociodemographic and socioeconomic groups, that historically have less access to health care, would have greater risk of presenting blind.

## **METHODS**

This was a retrospective cross-sectional study using patients from the Duke Ophthalmic Registry (DOR), which consisted of adults at least 18 years of age with glaucoma who were evaluated at the Duke Eye Center or its satellite clinics from 2012 to 2019. The Duke University Institutional Review Board approved this study with a waiver of informed consent because of the retrospective nature of this work. All methods adhered to the tenets of the Declaration of Helsinki for research involving human subjects and were conducted in accordance with regulations of the Health Insurance Portability and Accountability Act.

Information on comprehensive ophthalmic examinations from baseline and follow-up visits were collected including patient diagnosis codes (*International Classification* of Diseases [ICD]), procedures (*Current Procedural Terminol*ogy [CPT]), medications, and laboratory tests. Intraocular pressure (IOP) measured using the Goldmann applanation tonometry (Haag-Streit) and the Tono-Pen (Reichert, Inc) were also extracted from the database. Standard automated perimetry tests were acquired with the Humphrey field analyzer (Carl Zeiss Meditec, Inc) during the study period. Only 24-2 and 30-2 Swedish Interactive Threshold Algorithm or full threshold tests of the Humphrey field analyzer with size III white stimulus were exported from the database. Visual fields were excluded if they had >33% fixation losses or >15% false positives.

Patients were included if they had a diagnosis of glaucoma based on ICD codes upon first encounter to a Duke Eye Center glaucoma clinic. Additionally, the patients were classified as having primary open-angle glaucoma (POAG) or other glaucomas based on ICD codes. Patients were required to have a minimum of 1 good-quality visual field or best-corrected visual acuity measure recorded within 90 days of a first glaucoma encounter (defined as the baseline visit). They were excluded if they had a concurrent disease (identified using ICD codes) that could be affecting their vision, including an intraocular tumor, optical neuritis or other nonglaucomatous optic nerve and visual pathway disease, retinal detachment, endophthalmitis, amblyopia, agerelated macular degeneration, and if they had prior photocoagulation. Details of the codes used for classification, inclusion, and exclusion criteria have been published previously.<sup>19,20</sup>

• CLASSIFICATION OF BLINDNESS: Blindness was defined at the patient level and classified using the United States Social Security Administration's definition of legal blindness.<sup>21</sup> This definition specifies legal blindness as central visual acuity  $\leq 20/200$  with correction or a visual field mean deviation  $\leq -22$  dB in the better eye. This definition has been used before in glaucoma research studies.<sup>22,23</sup> Visual fields and visual acuity were collected within a 180-day window around the baseline encounter. Mean deviation values from 30-2 and 24-2 visual fields were used.

• **RISK FACTORS:** The demographic risk factors studied included gender (male vs female), race (African American / Black vs White), marital status (single vs married), age, income level, and education.

Race, gender, and marital status were self-reported. African American / Black and White were the only races included in the analysis because of the population of patients seen at the Duke Eye Center and statistical considerations related to power. Single marital status included divorced and widowed. Income level and education were obtained from United States Census Bureau's American Community Survey for 2006-2011. Income level was measured by the per capita income in the past 12 months and was race specific. Education was measured by the percentage of residents who achieved a high school education and was sex specific. Census data were assigned to patients based on the zip code they lived in. It is important to note that the income and education variables were not patient specific because they were aggregated using the patient's zip code. Although this loss in granularity is a limitation for the analysis, it has been shown to be an acceptable alternative to patient-level socioeconomic data.<sup>24</sup>

Descargado para Eilyn Mora Corrales (emorac17@gmail.com) en National Library of Health and Social Security de ClinicalKey.es por Elsevier en junio 16, 2023. Para uso personal exclusivamente. No se permiten otros usos sin autorización. Copyright ©2023. Elsevier Inc. Todos los derechos reservados.

TABLE 1. Summary	y Statistics for Stud	y Cohort Overall and	Across Blindness Status
------------------	-----------------------	----------------------	-------------------------

	All	Legally Blind	Not Blind	
Variable	(N = 3753)	(n = 192; 5%)	(n = 3561; 95%)	Р
Average SAP MD (dB)	-8.85 (8.10)	-26.8 (4.34)	-8.06 (7.27)	<.001
Gender, male, n (%)	1749 (47)	95 (49)	1654 (46)	.456
Race (African American / Black), n (%)	1654 (44)	125 (65)	1529 (43)	<.001
Marital status (single), n (%)	1427 (43)	93 (55)	1334 (42)	.001
Glaucoma type (other), n (%)	1998 (53)	107 (56)	1891 (53)	.525
Baseline age (y)	66.20 (13.95)	66.16 (16.14)	66.20 (13.83)	.971
Average IOP (mm Hg)	18.06 (6.62)	19.89 (8.73)	17.96 (6.47)	.003
Diabetes, n (%)	359 (10)	35 (18)	324 (9)	<.001
Annual income (per \$10 000)	2.99 (1.63)	2.4 (1.56)	3.02 (1.63)	<.001
Education (per 10%)	85.58 (12.71)	80.62 (15.39)	85.83 (12.51)	<.001

IOP = intraocular pressure, MD = mean deviation, SAP = standard automated perimetry.

Summaries are mean and SD, unless otherwise noted. All summaries are presented at the initial presentation to the Duke Eye Center. *P* values represent hypothesis tests across blindness status, with categorical variables using the  $\chi^2$  test, and continuous variables using the *t* test.

The clinical risk factors included baseline IOP (measured in mm Hg and averaged between the left and right eye) and history of diabetes as some studies suggest that patients with diabetes are at an increased risk for glaucoma.<sup>25,26</sup> History of diabetes was determined by presence of an *ICD* code for diabetes before the baseline visit date (*ICD-9*: 249, 250; *ICD-10*: E08-13). Baseline standard automated perimetry mean deviation was excluded because it was a measurement used to define the blindness outcome.

• STATISTICAL ANALYSES: In this analysis, we investigated the effect of the previously mentioned risk factors on presenting blind to the Duke Eye Center from a diagnosis of glaucoma. Univariable and multivariable logistic regressions were performed using the blindness indicator as the outcome variable. The associations of the risk factors with blindness were presented with ORs and 95% CIs for both the univariable and multivariable models. Models are presented overall and within glaucoma diagnosis type, POAG, and other glaucoma. Finally, the overall performance of the models was evaluated using the area under the receiver operating characteristic (ROC) curve (AUC). Any risk factors that had missing values were imputed using multiple imputation with 5 imputed datasets using the "mice" package in R.<sup>27</sup>

The summaries for the cohort are presented with continuous variables presented as mean and SD and categorical variables presented as counts and percentages. Patient data were anonymized, and all statistical analyses were conducted using the R programming language (version 3.5.1; R Core Team) within the Protected Analytics Computing Environment (PACE). PACE is a secure virtual network space developed by Duke University for analysis of identifiable protected health information. The type 1 error was set at 0.05 throughout.

## RESULTS

Our cohort consisted of 3753 glaucoma patients. Of these, 1755 (47%) had POAG and 1998 (53%) had other types of glaucoma, with a total of 192 (5%) patients presenting with legal blindness at their first visit. Of these 192 patients, 112 presented blind by visual acuity, 78 by visual field, and 2 by both metrics. Table 1 presents baseline demographic and clinical characteristics for this cohort. Overall, the mean (SD) age was 66.2 (13.6) years, 1749 subjects (47%) were male, 1654 (44%) self-identified as African American / Black, and 1427 (43%) were single. The average income in ten-thousand dollars was 3.0 (1.6), and the average percentage of residents receiving a high school education was 85.6% (12.7%). The mean average IOP was 18.1 (6.6) mm Hg and 359 (10%) of patients had a prior diabetes diagnosis. Only marital status (11%), income (14%), and education (13%) had missing values, with missingness in an appropriate range for multiple imputation.

Compared to the patients who did not present blind, the blind cohort had a greater proportion of African American / Black patients (65% vs 43%), single patients (55% vs 42%), and patients with a history of diabetes (18% vs 9%). Additionally, the blind cohort had a higher mean average IOP, 19.9 (8.7) mm Hg, compared with the not-blind cohort, at 18.0 (6.5) mm Hg. Finally, the blind cohort had a lower average annual income in ten-thousand dollars, 2.4 (1.6) compared to 3.0 (1.6), and a lower average percentage of residents receiving a high school education, 80.6 (15.6) compared to 86.8 (12.5).

Table 2 and Figure 1 display the results for the univariable and multivariable logistic regression models for all patients. In univariable models, all variables were significant (P < .05) for predicting presentation of blindness except for gender, glaucoma type, and age. African American / Black race

Variable	Univariable		Multivariable	
	OR (95% CI)	Р	OR (95% CI)	Р
Gender (male)	1.13 (0.84, 1.51)	.412	1.19 (0.87, 1.63)	.266
Race (African American / Black)	2.48 (1.83, 3.36)	<.001	1.81 (1.24, 2.64)	.002
Marital status (single)	1.74 (1.25, 2.44)	.002	1.45 (1.01, 2.08)	.050
Glaucoma type (other)	0.90 (0.67, 1.20)	.478	0.90 (0.67, 1.22)	.507
Age (per 10 y)	1.00 (0.90, 1.11)	.967	1.10 (0.99, 1.23)	.087
Average IOP (per 1 SD)	1.29 (1.13, 1.46)	<.001	1.22 (1.07, 1.39)	.003
Diabetes (yes)	2.23 (1.52, 3.27)	<.001	1.68 (1.13, 2.50)	.011
Annual income (per \$10 000)	0.75 (0.65, 0.86)	<.001	0.95 (0.80, 1.12)	.558
At least high school education (per 10%)	0.77 (0.69, 0.85)	<.001	0.86 (0.75, 0.98)	.028

#### TABLE 2. Univariable and Multivariable Logistic Regression Models for All Patients.

IOP = intraocular pressure, OR = odds ratio.

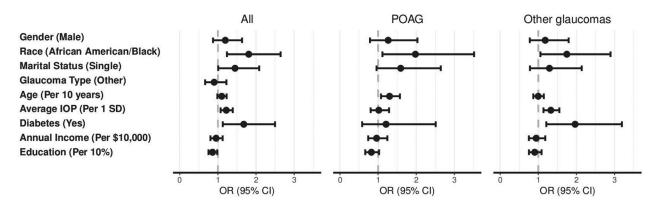


FIGURE 1. Forest plot demonstrating the odds ratios (ORs) and 95% CIs from the multivariable logistic regression models for all patients (left), primary open angle glaucoma (POAG) patients only (middle), and patients with other glaucoma types (right). IOP = intraocular pressure.

(OR 2.48, 95% CI 1.83-3.36), single marital status (OR 1.74, 95% CI 1.25-2.44), higher IOP (OR 1.29 per 1 SD higher, 95% CI 1.13-1.46), and prior diagnosis of diabetes (OR 2.23, 95% CI 1.52-3.27) were associated with a greater risk of presenting blind. Meanwhile, higher annual income (OR 0.75, 95% CI 0.65-0.86) and higher education (OR 0.77, 95% CI 0.69-0.85) were associated with lower risk of presenting blind. The associations found in the univariable models remained statistically significant and in the same direction in the multivariable logistic model, with an exception for annual income, which became insignificant. The AUC of the ROC curve for the overall multivariable model was 0.69 (Figure 2).

Table 3 displays the results of the univariable and multivariable logistic regression models for POAG patients. African American / Black race (OR 2.40, 95% CI 1.52-3.80), single marital status (OR 1.89, 95% CI 1.18-3.04), and a 10-year increase in age (OR 1.20, 95% CI 1.00-1.44) were associated with a greater risk of presenting blind. Meanwhile, higher annual income (OR 0.76, 95% CI 0.62-0.92) and higher education (OR 0.75, 95% CI 0.64-0.88) were associated with lower risk of presenting blind. Of these significant associations, only age and race remained significant in the multivariable model.

Table 4 displays the results of the univariable and multivariable logistic regression models for patients with other glaucoma diagnoses. In univariable models, all risk factors were significantly associated with blindness, except for gender and age, and maintained the same direction as in the models with all patients. In the multivariable model, the only variables that remained significant were African American / Black race (OR 1.75, 95% CI 1.06-2.89), higher IOP (OR 1.33 per 1 SD higher, 95% CI 1.14-1.55), and a prior diagnosis of diabetes (OR 1.96, 95% CI 1.21-3.19). The AUC of the ROC curve of the multivariable model was 0.68 for POAG and 0.70 for other glaucomas (Figure 2).

## DISCUSSION

In this study, we identified sociodemographic, socioeconomic, and clinical risk factors for presenting with blind-

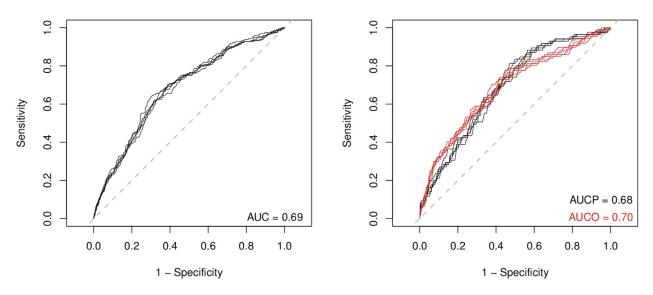


FIGURE 2. Receiver operating characteristic (ROC) curves showing the ability of the predicted probabilities of blindness derived from the multivariable logistic regression model to discriminate cases and controls. The panel on the left is for all patients whereas on the right there are curves for primary open angle glaucoma (POAG; black) and other glaucoma (red) patients. The area under the ROC curve (AUC) for the 3 models is 0.69, 0.68, and 0.70, respectively. Note that each curve is comprised of 5 curves from the multiple imputation. AUCP = AUC for POAG; AUCO = AUC for other glaucoma types.

	Univariable		Multivariable	
Variable	OR (95% CI)	Р	OR (95% CI)	Р
Gender (male)	1.18 (0.76, 1.83)	.451	1.26 (0.79, 2.03)	.332
Race (African American / Black)	2.40 (1.52, 3.80)	<.001	1.98 (1.11, 3.52)	.021
Marital status (single)	1.89 (1.18, 3.04)	.009	1.59 (0.96, 2.64)	.074
Age (per 10 y)	1.20 (1.00, 1.44)	.049	1.30 (1.08, 1.57)	.006
Average IOP (per 1 SD)	1.02 (0.81, 1.29)	.846	1.02 (0.80, 1.29)	.886
Diabetes (yes)	1.50 (0.73, 3.07)	.265	1.21 (0.58, 2.51)	.612
Annual income (per \$10 000)	0.76 (0.62, 0.92)	.007	0.96 (0.74, 1.24)	.756
At least high school education (per 10%)	0.75 (0.64, 0.88)	.001	0.82 (0.66, 1.03)	.096

#### TABLE 3. Univariable and Multivariable Logistic Regression Models for Patients With POAG

TABLE 4. Univariable and Multivariable Logistic Regression Models for Patients With Other Glaucoma Types

	Univariable		Multivariable	
Variable	OR (95% CI)	Р	OR (95% CI)	Р
Gender (male)	1.10 (0.74, 1.62)	.640	1.18 (0.78, 1.79)	.436
Race (African American / Black)	2.56 (1.70, 3.84)	<.001	1.75 (1.06, 2.89)	.031
Marital status (single)	1.64 (1.04, 2.59)	.038	1.29 (0.78, 2.14)	.323
Age (per 10 y)	0.91 (0.80, 1.04)	.161	1.00 (0.87, 1.14)	.974
Average IOP (per 1 SD)	1.43 (1.23, 1.67)	<.001	1.33 (1.14, 1.55)	<.001
Diabetes (yes)	2.68 (1.69, 4.27)	<.001	1.96 (1.21, 3.19)	.006
Annual income (per \$10 000)	0.75 (0.63, 0.89)	.002	0.94 (0.75, 1.18)	.613
At least high school education (per 10%)	0.78 (0.68, 0.90)	.001	0.90 (0.75, 1.09)	.284

#### American Journal of Ophthalmology

ness to a tertiary glaucoma clinic. Overall, the incidence of blindness at presentation was relatively low at 5% and did not appear to differ between the patients with POAG and other glaucoma. When all patients with primary or secondary glaucoma were analyzed in a multivariable model, African American / Black race, higher IOP, history of diabetes, and sociodemographic characteristics such as single marital status and lower education level were significant risk factors for blindness on first presentation at the Duke Eye Center.

When POAG was analyzed separately from other subtypes of glaucoma, our results demonstrated potential differences in risk factors for blindness for each diagnostic group. Although race was a significant predictor of blindness in a multivariable model for both POAG and other glaucomas, higher IOP and history of diabetes were significant for other glaucomas but not POAG. Meanwhile, a 10-year increase in age was a significant predictor in presenting blind in a multivariable model for POAG but not other glaucomas. This can be expected, as there are some aggressive glaucomas associated with secondary disorders that may cause blindness in younger patients, whereas POAG has been shown to be an age-related disease.<sup>28,29</sup>

In our multivariable models, higher IOP at presentation was significant in predicting blindness for other glaucomas but not POAG. There is indisputable high-level evidence that higher IOP increases the risk of conversion to and deterioration of all types of glaucoma but the fact that IOP was less of a predictor in POAG than other glaucomas in our models can be explained. POAG is often diagnosed and treated by comprehensive ophthalmologists and optometrists, and some patients may be referred to a specialist only if the condition is refractory to treatment. Because the Duke Eye Center is a tertiary glaucoma service, it is likely that many patients most likely came with some degree of IOP-lowering interventions. Secondary glaucomas, however, tend to have higher IOP than POAG, and thus, in these patients it follows that a higher IOP is associated with a greater risk of presenting blind. Additionally, this might also reflect previous data indicating that some eyes with POAG can progress and potentially go blind despite lower levels of IOP.<sup>30</sup>

The results of our study also indicated that a history of diabetes was not a significant predictor of presenting blind for POAG but was significant for other glaucomas. This may be because other glaucomas included neovascular glaucoma, a very severe form of glaucoma where patients frequently present blind. Our study included 283 patients with neovascular glaucoma, of whom 11% were blind on presentation. Of these 283 patients, 30% had a record of having diabetes.

Importantly, our study suggests that sociodemographic characteristics also play a significant role in presenting with blindness from glaucoma. For both POAG and other glaucomas, African American / Black race was a significant predictor of presenting blind in multivariable models. However, it is important to note that this does not necessarily indicate that race itself is associated with blindness. Instead, the race variable may be measuring other socioeconomic factors that are more directly associated with presenting already blind.

In this study, annual income and education were included to explain differences in blindness risk. These variables were significant in predicting blindness in the univariable models for both POAG and other glaucomas. However, they did not remain significant in multivariable models whereas race did, indicating that they cannot explain the entire association between race and blindness. This may be because annual income and education level were crudely measured at the zip code level instead of patientlevel. Thus, our adjustment for health disparity was not precise enough to explain the racial disparities in presenting blind.

Furthermore, there may be other variables that are associated with race such as access to care, medical education, and structural racism that could explain the association between race and blindness. This would be in line with what is known for most chronic diseases. In general, chronic diseases like glaucoma require access to specialized medical care, frequent ancillary testing, and expensive medical and surgical interventions. Although the effect of indirect or nonmedical costs can be more difficult to quantify, they are no less of a burden and negatively impact adherence to treatment.<sup>31,32</sup>

As subjects develop further into the disease course, they increasingly rely on support systems such as immediate family for office visits and use of medication. Additionally, because glaucoma is a silent, chronic disease, continued patient trust in doctors is vital for successful treatment. Yet, factors such as racial bias and the history of medical trauma in the Black community has been linked to eroded trust within Black patients, leading to lower adherence to treatment.<sup>33,34</sup> Finally, it has been proposed that chronic stress from racism may play a role in cardiovascular risk factors related to glaucoma.<sup>35</sup> Thus, structural racism may play a significant role in the disparity between Black and White patients.<sup>36</sup>

Higher-level education is also strongly linked to better health and determinants of health, such as health behaviors, preventative service use, and patient empowerment and advocacy.<sup>37,38</sup> This is especially significant for a disease like glaucoma, which is asymptomatic early on. However, because patients with low education are less likely to engage in preventative service use, they are more likely to present late for diagnosis and have a higher risk of progressing to blindness by the time they reach a tertiary center like Duke.<sup>39</sup> Our study highlights the influence of such socioeconomic variables in glaucoma care and the historical necessity to ensure that racial minorities and socioeconomically disadvantaged patients are properly educated about and have adequate access to eye care.

Our study did have limitations. For example, although we did have a large retrospective cohort, the data had missing values that required imputation. Nonetheless, the percentage of missingness was only in 3 risk factors, and less than 16% and the multiple imputation approach should be sufficient.<sup>40</sup> Additionally, there are limitations associated with the use of *ICD* codes to determine glaucoma diagnosis. This is because *ICD* codes are used for billing, not making diagnoses. As a result, there may be some coding errors in our data set, impacting the overall reliability of our data.

Furthermore, there was a lack of stratification between newly diagnosed glaucoma and previously diagnosed glaucoma within our data. Thus, we cannot be sure how long patients have had a glaucoma diagnosis before presenting to the clinic. However, because our study defines the baseline visit as the first encounter with the clinic, and not the first diagnosis of glaucoma, we are able to minimize the impact of this limitation.

Finally, because we defined our cohort as the first encounter to the glaucoma clinic, the visual fields used to define blindness may be impacted by the known learning effect associated with initial visual field testing. However, it is reasonably expected that most patients with glaucoma referred for tertiary care have had some experience with visual field testing with their primary providers, and only 182 (5%) patients were excluded because of a lack of a good quality visual field or best-corrected visual acuity measure.

There are also limitations associated with the demographic data used in the study. In particular, the demographic factors of annual income and education were crudely calculated by zip code as patient-specific data were not available. Additionally, in the clinical data, 24-2 visual field tests were used in addition to 30-2 as defined by the US SSA for the definition of blindness. The effect of this is likely small as studies have shown that 24-2 visual field tests provide comparable information to 30-2 visual field tests.<sup>41</sup> Finally, patients with substantial visual impairment or blindness are also often referred to specialized care for appropriate vision rehabilitation. Because Duke is a tertiary referral center, the patient population may not generalize to all glaucoma patient populations.

In conclusion, our study highlights the effect of clinical, sociodemographic, and socioeconomic variables on presentation of blindness from glaucoma at a tertiary eye center. African American / Black race, higher IOP, history of diabetes, single marital status, and lower education level were significant risks factors for blindness on first presentation for all glaucomas. However, our study also suggests potential differences in risk factors for presenting blind between POAG and other glaucomas, with older age being a more significant risk factor for presenting blind from POAG, and higher IOP and history of diabetes being more significant in other types of glaucoma. Additionally, race was a significant risk factor for both POAG and other glaucomas, though this may be due to other socioeconomic and societal factors associated with race such as access to care, income, education, and racism. These findings underscore the importance of socioeconomic variables like education and income on presenting blind from glaucoma, highlighting the need for better education and care in disadvantaged communities.

Funding/Support: Research reported in this publication was supported by the National Eye Institute of the National Institutes of Health (Bethesda, Maryland) under Awards Number K99EY033027 (S.I.B.), R01EY029885 (F.A.M.), and R21EY031898 (F.A.M.).

Acknowledgments: Sayan Mukherjee would like to acknowledge partial funding from Human Frontier Science Program RGP005, National Science Foundation (NSF) DMS 17-13012, NSF BCS 1552848, NSF DBI 1661386, NSF IIS 15-46331, and NSF DMS 16-13261. We would also like to acknowledge funding from Duke University's Bass Connections Data+ Program.

## REFERENCES

- 1. Weinreb RN, Aung T, Medeiros FA. The pathophysiology and treatment of glaucoma: a review. JAMA. 2014;311:1901–1911.
- 2. Tham YC, Li X, Wong TY, Quigley HA, Aung T, Cheng CY. Global prevalence of glaucoma and projections of glaucoma burden through 2040. *Ophthalmology*. 2014;121:2081–2090.
- **3.** Quigley HA, Broman AT. The number of people with glaucoma worldwide in 2010 and 2020. *Br J Ophthalmol.* 2006;90:262–267.
- Holló G, Kóthy P, Géczy A, Vargha P. Personality traits, depression, and objectively measured adherence to once-daily prostaglandin analog medication in glaucoma. *J Glaucoma*. 2009;18:288–292.

- 5. Evans RL. Loneliness, depression, and social activity after determination of legal blindness. *Psychol Rep.* 1983;52(2):603–608.
- 6. Ip SPS, Leung YF, Mak WP. Depression in institutionalised older people with impaired vision. *Int J Geriatr Psychiatry*. 2000;15(12):1120–1124.
- 7. Klein GS. Blindness and isolation. Psychoanal Study Child. 1962;17.
- 8. Thurston M, Thurston A, McLeod J. Socio-emotional effects of the transition from sight to blindness. *Br J Visual Impair*. 2010;28(2):90–112.
- 9. Fitzgerald RG, Ebert JN, Chambers M. Reactions to blindness: a four-year follow-up study. *Percept Mot Skills*. 1987;64(2):363–378.

Financial Disclosures: The sponsor or funding organization had no role in the design or conduct of this research. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health. F.A.M. received support from Aerie Pharmaceuticals (Consultant; C), Allergan (C, Financial Support; F), Annexon (C), Biogen (C), Carl Zeiss Meditec (C, F), Google Inc. (F), Heidelberg Engineering (F), nGoggle Inc. (Patent; P), Novartis (F), Stealth Biotherapeutics (C), Stuart Therapeutics (C), and Reichert (C, F). All other authors indicate no financial support or financial conflict of interest. All authors attest that they meet the current ICMJE criteria for authorship.

Descargado para Eilyn Mora Corrales (emorac17@gmail.com) en National Library of Health and Social Security de ClinicalKey.es por Elsevier en junio 16, 2023. Para uso personal exclusivamente. No se permiten otros usos sin autorización. Copyright ©2023. Elsevier Inc. Todos los derechos reservados.

- 10. Legood R. Are we blind to injuries in the visually impaired? A review of the literature. *Inj Prev.* 2002(2):155–160.
- Hamedani AG, VanderBeek BL, Willis AW. Blindness and visual impairment in the Medicare population: disparities and association with hip fracture and neuropsychiatric outcomes. *Ophthalmic Epidemiol.* 2019;26(4):279–285.
- Crews JE, Chou CF, Sekar S, Saaddine JB. The prevalence of chronic conditions and poor health among people with and without vision impairment, aged ≥65 years, 2010–2014. Am J Ophthalmol. 2017;182:18–30.
- Frick KD, Gower EW, Kempen JH, Wolff JL. Economic impact of visual impairment and blindness in the United States. *Arch Ophthalmol.* 2007;125(4):544–550.
- Tatham AJ, Medeiros FA, Zangwill LM, Weinreb RN. Strategies to improve early diagnosis in glaucoma. *Prog Brain Res.* 2015;221:103–133.
- **15.** Murakami Y. Racial and ethnic disparities in adherence to glaucoma follow-up visits in a county hospital population. *Arch Ophthalmol.* 2011;129(7):872–878.
- Javitt JC, McBean AM, Nicholson GA, Babish JD, Warren JL, Krakauer H. Undertreatment of glaucoma among Black Americans. N Engl J Med. 1991;325(20):1418–1422.
- 17. Chen PP. Risk and risk factors for blindness from glaucoma. *Curr Opin Ophthalmol.* 2004;15:107–111.
- Williams AM, Huang W, Muir KW, Stinnett SS, Stone JS, Rosdahl JA. Identifying risk factors for blindness from primary open-angle glaucoma by race: a case–control study. *Clin Ophthalmol.* 2018;12:377–383.
- Berchuck S, Jammal A, Mukherjee S, Somers T, Medeiros FA. Impact of anxiety and depression on progression to glaucoma among glaucoma suspects. Br J Ophthalmol. 2021;105:1244–1249.
- Jammal AA, Thompson AC, Mariottoni EB, et al. Rates of glaucomatous structural and functional change from a large clinical population: the Duke Glaucoma Registry Study. *Am J Ophthalmol.* 2021;222:238–247.
- US Social Security Administration. Understanding Supplemental Security Income SSI Eligibility Requirements, 2022 Edition. (Accessed December 12, 2022), 2023. https://www.ssa.gov/ssi/text-eligibility-ussi.htm.
- Saunders LJ, Russell RA, Kirwan JF, McNaught AI, Crabb DP. Examining visual field loss in patients in glaucoma clinics during their predicted remaining lifetime. *Invest Opthalmol Vis Sci.* 2014;55 102-102.
- Heijl A, Aspberg J, Bengtsson B. The effect of different criteria on the number of patients blind from open-angle glaucoma. BMC Ophthalmol. 2011;11:31.
- 24. Geronimus AT, Bound J. Use of census-based aggregate variables to proxy for socioeconomic group: evidence from national samples. *Am J Epidemiol.* 1998;148:475–486.
- 25. Bonovas S, Peponis V, Filioussi K. Diabetes mellitus as a risk factor for primary open-angle glaucoma: a meta-analysis. *Diab Med.* 2004;21:609–614.

- Zhao D, Cho J, Kim MH, Friedman DS, Guallar E. Diabetes, fasting glucose, and the risk of glaucoma. *Ophthalmology*. 2015;122:72–78.
- Buuren SV, Groothuis-Oudshoorn K. mice: multivariate imputation by chained equations in R. J Stat Softw. 2011;45(3).
- Nouri-Mahdavi K, Hoffman D, Coleman AL, et al. Predictive factors for glaucomatous visual field progression in the Advanced Glaucoma Intervention Study. *Ophthalmology*. 2004;111:1627–1635.
- 29. Heijl A. Reduction of intraocular pressure and glaucoma progression. Arch Ophthalmol. 2002;120 1268-1268.
- Susanna BN, Ogata NG, Jammal AA, Susanna CN, Berchuck SI, Medeiros FA. Corneal biomechanics and visual field progression in eyes with seemingly well-controlled intraocular pressure. *Ophthalmology*. 2019;126:1640–1646.
- Newman-Casey PA, Niziol LM, Gillespie BW, Janz NK, Lichter PR, Musch DC. The association between medication adherence and visual field progression in the Collaborative Initial Glaucoma Treatment Study. *Ophthalmology*. 2020;127(4):477–483.
- 32. Rossi GCM, Pasinetti GM, Scudeller L, Radaelli R, Bianchi PE. Do Adherence Rates and Glaucomatous Visual Field Progression Correlate? *Eur J Ophthalmol.* 2011;21:410–414.
- Gamble VN. Under the shadow of Tuskegee: African Americans and health care. Am J Public Health. 1997;87:1773–1778.
- Silverman-Lloyd LG, Bishop NS, Cerdeña JP. Race is not a risk factor: reframing discourse on racial health inequities in CVD prevention. Am J Prev Cardiol. 2021;6:100185.
- Huck A, Harris A, Siesky B, et al. Vascular considerations in glaucoma patients of African and European descent. Acta Ophthalmol. 2014;92:e336–e340.
- **36.** Cabrera MT, Chen A. It's time we reform our perspectives on race and glaucoma. *Transl Vis Sci Technol.* 2022;11(9):22.
- Cutler DM, Lleras-Muney A. Understanding differences in health behaviors by education. J Health Econ. 2010;29(1):1–28.
- Fletcher Jason M, Frisvold David E. Higher education and health investments: does more schooling affect preventive health care use? J Hum Cap. 2009;3:144–176.
- Javitt JC. Preventing blindness in Americans: the need for eyehealth education. Surv Ophthalmol. 1995;40:41–44.
- 40. Jakobsen JC, Gluud C, Wetterslev J, Winkel P. When and how should multiple imputation be used for handling missing data in randomised clinical trials – a practical guide with flowcharts. BMC Med Res Methodol. 2017;17(1):162.
- Khoury JM, Donahue SP, Lavin PJ, Tsai JC. Comparison of 24-2 and 30-2 perimetry in glaucomatous and nonglaucomatous optic neuropathies. J Neuroophthalmol. 1999;19(2):100–108.