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Racial, ethnic, and socioeconomic disparities in glaucoma onset and severity in a diverse nationwide cohort in the United States

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Abstract

Purpose: To analyze patterns of diagnosis coding usage and validate epidemiologic patterns of glaucoma onset and severity among primary glaucoma patients within the National Institutes of Health *All of Us* database.

Patients and Methods: We used ICD diagnosis codes to build 4 cohorts of patients with mild, moderate, severe, and unspecified stage glaucoma (N = 2982). Descriptive analyses were stratified by disease stage, and mean age at diagnosis was compared across racial and ethnic groups. Multivariable ordinal regression was used to examine risk factors for increasing glaucoma severity.

Results: Of 2982 participants, 1714 (57%) had unspecified severity staging. Black/African Americans and other races were diagnosed with glaucoma at significantly younger ages compared to Whites (means 60 and 60 vs. 66 years; p<0.001). Hispanic/Latino participants also had an earlier mean age of diagnosis (61 vs. 65 years; p=0.001). Black/African Americans had higher odds of more severe glaucoma (OR: 2.20, 95% CI: 1.62 – 3.30; p<0.001) than Whites when adjusting for socioeconomic characteristics.

Conclusions: Black, Hispanic/Latino, and other minority participants are diagnosed with glaucoma at younger ages, and Blacks are more likely to be diagnosed with moderate-to-severe glaucoma. These findings validate prior population-based studies. Furthermore, we observed a gap in the use of diagnosis codes, as only 43% of participants had a specified severity stage in this national cohort. This may have implications for large-scale observational research concerning glaucoma severity as electronic health records and claims databases typically lack other measures of disease progression, such as imaging and visual field data.

Precis

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Racial/ethnic minorities are diagnosed with glaucoma at younger ages, and Blacks are more likely to be diagnosed with moderate-to-severe glaucoma. Additionally, we highlight a gap in the use of diagnosis codes.

Introduction

Several studies have reported racial and ethnic disparities among patients with primary glaucoma with Blacks, Hispanics, and Asians having increased severity of disease at the time of diagnosis and more rapid progression when compared to their White counterparts.[1–6] While associations between demographics and severity of disease have been explored, these relationships are complicated by the impact of other socioeconomic characteristics that are not easily controlled such as insurance status, education level, annual income, language, and access to technology.[7] Moreover, prior research has limitations due to geographic location and cohort size.[1–6] With the expansion of electronic health record (EHR) data, there now is access to larger data sources such as the National Institutes of Health (NIH) *All of* Us Research Program database, the American Academy of Ophthalmology Intelligent Research In Sight (IRIS) Registry, and claims data that allow analysis of these associations on a national scale. Of these, the NIH *All of Us* database has the unique advantage of containing data regarding socioeconomic characteristics and patient-reported outcomes through their surveys and focused recruitment of populations traditionally underrepresented in biomedical research.[8,9]

Though these databases have yet to connect patient demographics with clinical measurements including optical coherence tomography (OCT), fundus photography, and visual field (VF) testing, their findings can be compared with prior literature monitoring progression of disease using diagnosis codes and surgery rates.[1–3,5,10,11] As surgery rates may vary by surgeon, diagnosis coding offers another option for monitoring disease progression. However, there has been inconsistent use and accuracy of International Classification of Disease (ICD) coding in prior studies.[12–15] Thus, even this measure requires validation in a new dataset, such as the *All of Us* database.

In this study, we analyze patterns of diagnosis code usage and validate known epidemiologic patterns in the newest version of the NIH *All of Us* national database. Socioeconomic characteristics are then correlated with the severity of glaucomatous disease with the goal of developing improved healthcare interventions to combat health disparities among patients with glaucoma.

Methods

Data were obtained from the 6th version of the NIH *All of Us* Research Program, a national database with the goal of enrolling 1 million individuals from communities traditionally underrepresented in biomedical research.[9] At the time of the analysis, over 412,000 participants had enrolled and completed the initial steps of the program, and more than 80% were from these communities.[8] Institutional Review Board approval was obtained and participants provide written informed consent upon enrollment in the *All of* Us program. Patient information was de-identified through a series of data transformations prior to being

made available to researchers. This study consisted of a secondary analysis of de-identified data available on the *All of Us* Researcher Workbench. This secondary analysis was not considered human subjects research based on determination by the University of California San Diego Institutional Review Board. The project adhered to the tenets of the Declaration of Helsinki.

ICD-9 and 10 coding was used to build 4 cohorts: patients with mild glaucoma, moderate glaucoma, severe glaucoma, and unspecified stage glaucoma (total N = 2982). Diagnosis codes used for defining these cohorts are detailed in Supplemental Table 1. Individuals with multiple diagnoses encompassing more than one severity stage were placed in the cohort corresponding to the highest level of severity documented.

Descriptive analyses were performed for the total cohort including mean age at time of study, mean and binned age of first diagnosis, sex, race, ethnicity, education, annual income, and insurance status using Analysis of Variance (ANOVA) for continuous variables and Pearson's Chi-square tests for categorical variables. With the exception of age, demographic information was solicited from a basic health information survey completed by all participants and categories reflect *All of Us* reporting. In accordance with the NIH *All of Us* Research Program Data and Statistics Dissemination Policy, counts of 20 or less and corresponding percentages cannot be displayed. In some cases, data were collapsed to account for this, and percentages may not equal 100 due to participants skipping or choosing not to answer the question. Binned age was placed into the following groups chosen prior to analysis: 18 – 40, 41 – 50, 51 – 60, 61 – 70, 71 – 80, and 81 and older. Sex was determined based on participants' response to a survey question regarding their sex assigned at birth, where options were male, female, intersex, none of these, prefer not to answer, or skip; due to limited data, only values for male and female responses were included. Participants identified their race from options including White, Black, Asian, or Other; due to limited data and compliance with the *All of Us* Data and Statistics Dissemination policy, Asian was combined with Other for the analysis. In accordance with participants' responses to a survey regarding ethnicity, ethnicity was categorized as Hispanic or Latino or not Hispanic or Latino. Education level was categorized according to participants' responses to a survey which categorized years of school as One through Four, Five through Eight, Nine through Eleven, Twelve or GED, College One to Three, College Graduate, Advanced Degree, or Prefer Not to Answer; these data were collapsed into categories of High school degree/GED or less, Some college, or College graduate or advanced degree due to limited data. Income was categorized based on responses to a survey question and included $25,000 or less, $25,000 – $50,000, $50,000 – $100,000, $100,000 – $200,000, > $200,000. Insurance was categorized in a survey question as Medicare, Medicaid, VA, Military, Employer or Union, Purchased, or Other Health Plan, and we collapsed these to Medicaid, Medicare, VA/Military, and Other due to limited data. The same analysis was performed for each cohort and then performed post-hoc tests excluding participants in the unspecified stage cohort in order to correlate disease severity with demographic characteristics. Post-hoc tests also were performed to compare age of diagnosis across race groups and ethnicity groups. Statistical significance was defined at α level less than 0.05 for all analyses.

We selected 31 questions relating to healthcare access and barriers to care from the NIH *All of Us* Research Program Healthcare Access and Utilization Survey (HCAUS) prior to analysis, and answers were collapsed into binary categories. Participant answers to these questions were separated by cohort and limited to those in the mild, moderate, and severe glaucoma cohorts (N = 1268). Participants from the unspecified stage cohort were removed to prevent potential interference when correlating with disease severity. To remain in accordance with the NIH *All of Us* Research Program's Data and Statistics Dissemination Policy, any questions returning a value of 20 or less were removed from the analysis. We performed Pearson's Chi-square test for the remaining six questions (listed in Supplemental Table 2).

A multivariable ordinal regression model was created to evaluate risk factors for increasing glaucoma severity, including the demographics and six selected HCAUS questions as covariates in the analysis. Missingness was calculated prior to analysis to be 7.8% overall. Data were imputed using the within-cohort mode for each categorical variable. The only continuous variable was age, which had no missing data, so imputation was not needed. Numerical variables were checked for high levels of correlation (correlation coefficient > 0.80), removing age at the time of study (correlated with age at diagnosis, r = 0.84) from the model. The model then was applied using the remaining variables to obtain the odds ratio, 95% confidence interval, and p-value for each covariate.

Results

Of the 2982 participants in our study, 1714 (57%) were given a diagnosis of primary glaucoma without a disease stage specified, 444 (15%) carried a diagnosis of mild glaucoma, 460 (15%) carried a diagnosis of moderate glaucoma, and 364 (12%) carried a diagnosis of severe glaucoma. The mean (SD) age of the total cohort at the time of their first glaucoma diagnosis was 63.7 (10.7) years, and the mean (SD) age at the time of the study was 71.8 (10.0) years. There were 1748 (59%) who identified as male and 1234 (41%) who identified as female. Of the total cohort, 2121 (71%) were White, 453 (15%) were Black/African American, and 408 (13.68%) indicated another race. 265 (9%) identified as Hispanic or Latino.

Table 1 summarizes the descriptive statistics for the total cohort and separated by disease severity. Blacks/African Americans and participants of other races were diagnosed with glaucoma at significantly younger ages than Whites (mean 60 and 60 vs 66; $p < 0.001$) (Figure 1). Participants identifying as Hispanic or Latino were also diagnosed at a significantly younger age than non-Hispanic or Latino participants (mean 61 vs 65; $p = 0.001$). As expected, glaucoma severity was also significantly different between participants under 40 years old and participants over 80 years old.

Table 2 outlines the results of our multivariable ordinal regression model of glaucoma severity, which showed Black/African American participants had significantly higher odds (OR: 2.20; 95% CI: 1.62 – 3.00) of carrying a more severe glaucoma diagnosis than White participants when controlling for other covariates and potential barriers to care (Figure 2).

Discussion

In this study, we assessed epidemiologic patterns of glaucoma onset and severity among participants in the national NIH *All of Us* Research Program. Comparing our cohort by race and ethnicity, Black/African Americans and participants of other minority groups experienced significantly earlier incidence of glaucomatous disease when compared with their White counterparts. Moreover, Black/African American participants also had significantly higher odds of more severe disease.

Separating the cohort by race, participants from non-White racial backgrounds, including Black/African American participants, Asians, and other races, received their first glaucoma diagnosis on average six years earlier than their White counterparts, and Hispanic or Latino participants were diagnosed with glaucoma on average four years earlier than their non-Hispanic or Latino counterparts. These findings are consistent with prior literature reporting that Black, Asian, and Hispanic patients are often diagnosed at earlier ages and present with more severe disease on initial evaluation.[1,4,5,16] As such, the current findings validate epidemiologic patterns from prior population-based studies and help establish the credibility of using the NIH *All of Us* Research Program database for research in glaucoma.[17] The *All of* Us database provides the added benefit of allowing researchers to control for covariates that are traditionally not included in statistical models derived from other data sources, including socioeconomic characteristics and patient-reported barriers to care including medication costs and inability to afford specialized care. Most electronic databases, such as the IRIS Registry and claims data, do not include this information. Other databases have attempted to use proxies for these characteristics such as zip codes to estimate socioeconomic status,[18–20] but this is not equivalent to collecting information relating to visit and medication adherence directly from the patient, as has been shown in our previous studies utilizing the *All of Us* database.[21,22] We also found that race was an independent risk factor for glaucoma severity even when controlling for these socioeconomic characteristics, demographics, and variables related to healthcare access and utilization. This highlights the need for further research into risk conferred by anatomical and biological variation, such as recent studies regarding mitochondrial variants and increased remodeling of the lamina cribosa in Blacks/African Americans.[1,3,23,24]

In addition, our findings suggest that changes to standard practice patterns may be necessary to help narrow the disparities between these groups. Studies have shown that Blacks continue to undergo higher rates of surgery despite no evidence of a pattern of medication underuse when compared to Whites, [11] and the American Academy of Ophthalmology Primary Open-Angle Glaucoma Suspect Preferred Practice Patterns do not recommend increased screening or monitoring among any racial populations.[11,25] Given persistent evidence of earlier disease onset and greater odds of progression to severe disease in minority populations as highlighted by these data in *All of Us*, increased screening or monitoring among high-risk populations to improve outcomes should be further considered.[26,27]

While controversy exists regarding the value of community-based glaucoma screening programs,[28–30] multiple studies have shown that these programs can significantly increase

patient retention rates, generate new revenue streams, and improve patient outcomes when utilized effectively.[31–33] Implementing strategies such as employing diverse healthcare teams, increasing representation in advertisements and educational materials, and partnering with community advisory boards to target the needs of the local community can help to foster trust in the healthcare among these groups and lead to greater healthcare engagement.[31] As such, we argue it may be indicated in all diverse communities—but especially important in predominantly Black/African American communities—to utilize these programs to promote earlier detection of glaucoma and encourage regular follow-up care to mitigate disease progression. In addition, artificial intelligence and telemedicine may also offer opportunities to expand access to eyecare by making glaucoma screening more accurate, efficient, accessible, and less costly to ethnic minority groups.[34]

We also found that 57% of participants did not have any glaucoma severity staging specified, highlighting a large gap in the utilization of ICD coding for documenting and monitoring glaucoma disease severity. Given the inconsistency of results in prior literature regarding the use and accuracy of diagnosis codes,[12–15] our data suggests the underutilization of ICD codes with specified severity staging is present on a national scale, which poses a challenge when analyzing patterns of disease progression and identifying disparities among patients. When used correctly, diagnosis coding provides the opportunity to conduct population health surveillance regarding diagnosis and treatment patterns.[35,36] However, clinicians are often forced to balance clinic efficiency, billing requirements, and visit documentation alongside patient care, resulting in non-specific diagnosis coding. Because ophthalmology is a high-volume specialty with intense time pressures,[37] it is understandable that precise diagnosis coding may not always be practically feasible.

One possible approach to addressing this issue is to develop support mechanisms in clinical information systems such as EHRs. For example, glaucoma severity could be staged automatically using quantitative criteria derived from visual fields and imaging data. This would require improved adoption of Data Imaging and Communications in Medicine (DICOM) standards, a well-documented challenge in ophthalmology,[38–40] as well as improved interoperability between ophthalmic imaging devices, picture archiving and communication systems (PACS), and EHRs, such that these data can seamlessly flow from the devices to the EHR systems to be integrated into diagnostic algorithms, creating a more objective measure when determining disease severity. This could lead to decision support mechanisms which would provide an automated suggested stage of disease, removing the burden on clinicians and standardizing coding of disease severity. Likewise, automated messaging systems could utilize patient disease severity to identify those patients requiring more frequent eye exams and send reminders as needed, which can improve visit and medication adherence in at-risk populations.[31] In this way, data interoperability could serve as a bridge for outreach to more patients with more severe disease and can help narrow disparities.

Our study had some limitations. Though the NIH *All of Us* Research Program provides an array of benefits, such as a large number of participants and information on various social and demographic factors relating to its participants, the data de-identification prevents researchers from obtaining additional information or clarification from study participants,

which can result in missing data and a lack of nuanced qualitative information. This limitation also applies to other national datasets and claims databases. Not all participants completed the optional surveys on healthcare access and utilization and social determinants of health, restricting our analysis to a limited set of questions in these areas (Supplemental Table 2). However, this limitation may become less pronounced as this database continues to enroll more participants, including more participants who answer these surveys. Despite this, *All of Us* is one of the only data sources where it is possible to analyze social determinants in tandem with EHR data.

In conclusion, this study found racial and ethnic minorities were diagnosed with glaucoma at significantly earlier ages, and Black/African American patients were more likely to carry a more severe glaucomatous disease diagnosis when compared to their White counterparts. Furthermore, more than half of participants with primary glaucoma in this national database did not have glaucoma severity staging specified. As we work to improve the accuracy and utilization of diagnosis codes in EHR data, there should be a focus on addressing significant health disparities through increased outreach and monitoring of at-risk populations.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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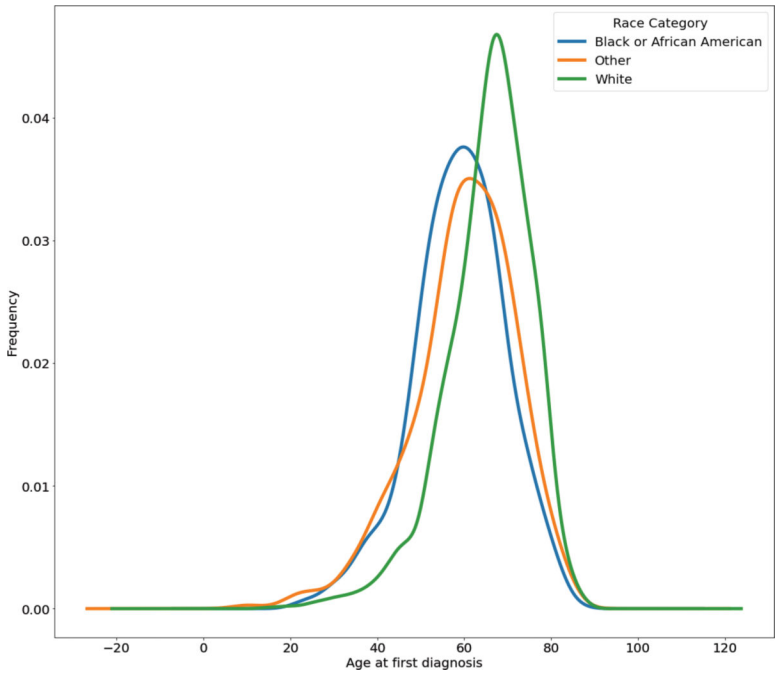

Figure 1.

Density plot showing the distribution of patient's age of first glaucoma diagnosis separated by race among the All of Us participants with glaucoma

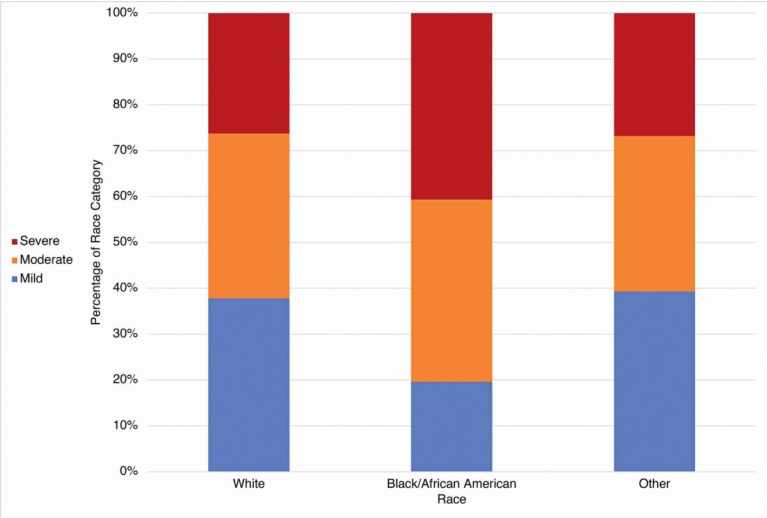

Figure 2.

Bar graph showing the distribution of glaucomatous disease severity levels by race among All of Us participants with glaucoma

Table 1.

Distribution of demographic characteristics and patient-reported barriers to care by disease stage among *All of Us* participants with glaucoma

	Total Cohort (N = 2982)	Mild (N = 444, 14.89%)	Moderate (N = 460, 15.43%)	Severe (N = 364, N = 12.21%)	Unspecified (N = 1714, 57.48%)	P values
	N (%)	N (%)	N (%)	N (%)	N (%)	
Mean age at study	71.78	71.55	72.92	73.38	71.19	< 0.001
Mean age at first glaucoma diagnosis	63.71	64.19	64.95	63.62	63.27	0.02
Age at first diagnosis						0.10
</= 50 *	292 (9.79%)	44 (9.91%)	35 (7.61%)	28 (7.69%)	185 (10.80%)	
51–60	702 (23.54%)	86 (19.59%)	89 (19.35%)	94 (25.82%)	433 (22.35%)	
61–70	1176 (39.44%)	185 (41.67%)	185 (40.22%)	141 (38.74%)	665 (38.80%)	
> 70 *	861 (28.87%)	128 (28.83%)	151 (32.83%)	101 (27.75%)	481 (28.06%)	
Sex						< 0.001
Male	1748 (58.62%)	214 (48.20%)	197 (42.83%)	178 (48.90%)	645 (37.63%)	
Female	1234 (41.38%)	230 (51.80%)	263 (57.17%)	186 (51.10%)	1069 (62.37%)	
Race						< 0.001
White	2121 (71.13%)	337 (75.90%)	320 (69.57%)	234 (64.29%)	1230 (71.76%)	
Black/African American	453 (15.19%)	41 (9.23%)	83 (18.04%)	85 (23.35%)	244 (14.24%)	
Other	408 (13.68%)	66 (14.86%)	57 (12.39%)	45 (12.36%)	240 (14.00%)	
Ethnicity						0.004
Hispanic or Latino	265 (8.89%)	30 (6.76%)	27 (5.87%)	29 (7.97%)	179 (10.44%)	
Not Hispanic or Latino	2717 (91.11%)	414 (93.24%)	433 (94.13%)	335 (92.03%)	1535 (89.56%)	
Education						0.07
High school degree/GED or less	446 (14.96%)	54 (12.16%)	64 (13.91%)	51 (14.01%)	277 (16.16%)	
Some college	721 (24.18%)	107 (24.43%)	100 (21.98%)	78 (21.55%)	436 (25.66%)	
College graduate or advanced degree	1787 (59.93%)	277 (63.24%)	291 (63.96%)	233 (64.36%)	986 (58.03%)	
Annual Income						0.03
$25,000 or less	473 (15.86%)	49 (12.83%)	67 (17.63%)	55 (17.74%)	302 (20.61%)	
$25,000 - $50,000	477 (16.00%)	66 (17.28%)	66 (17.37%)	54 (17.42%)	291 (19.86%)	
$50,000 - $100,000	772 (25.89%)	137 (35.86%)	108 (28.42%)	98 (31.61%)	429 (29.28%)	
$100,000 - $200,000	566 (18.98%)	93 (24.35%)	98 (25.79%)	69 (22.26%)	306 (20.89%)	
$200,000 or more	249 (8.35%)	37 (9.69%)	41 (10.79%)	34 (10.97%)	137 (9.35%)	
Insurance						< 0.001
Medicaid	266 (8.92%)	28 (6.31%)	28 (6.09%)	30 (8.24%)	180 (10.50%)	
Medicare	1134 (38.03%)	181 (40.77%)	185 (40.22%)	147 (40.38%)	621 (36.23%)	
VA/Military	130 (4.36%)	25 (5.63%)	31 (6.74%)	20 (5.49%)	54 (3.15%)	
Other insurance	928 (31.12%)	148 (33.33%)	144 (31.30%)	96 (26.57%)	540 (31.51%)	

	Total Cohort (N = 2982)	Mild (N = 444, 14.89%)	Moderate (N = 460, 15.43%)	Severe (N = 364, N = 12.21%)	Unspecified (N = 1714, 57.48%)	P values
	N (%)	N (%)	N (%)	N (%)	N (%)	
HCAUS Question	**Total Cohort (N = 1268)**	**Mild (N = 444, 35.02%)**	**Moderate (N = 460, 36.28%)**	**Severe (N = 364, N = 28.71%)**		**P values**
Reported needing eyeglasses but not getting them because they couldn't afford it within the last 12 months						0.59
Yes	89 (7.02%)	28 (6.31%)	32 (6.96%)	29 (7.97%)		
No	972 (76.66%)	342 (77.03%)	361 (78.48%)	269 (73.90%)		
Reported asking doctor for lower cost medication because they couldn't afford it within the last 12 months						0.18
Yes	233 (18.38%)	84 (18.92%)	72 (15.65%)	77 (21.15%)		
No	910 (71.77%)	318 (71.62%)	336 (73.04%)	256 (70.33%)		
Reported not seeing a specialist because they couldn't afford it within the last 12 months						0.34
Yes	70 (5.52%)	21 (4.73%)	24 (5.22%)	25 (6.87%)		
No	981 (77.37%)	343 (77.25%)	267 (79.78%)	271 (74.45%)		
Reported delaying medical care because they were paying out of pocket for part or all of the procedure within the last 12 months						0.90
Yes	100 (7.89%)	34 (7.66%)	35 (7.61%)	31 (8.52%)		
No	914 (72.08%)	321 (72.30%)	330 (71.74%)	263 (72.25%)		
Reported speaking to an eye doctor within the last 12 months						0.60
Yes	938 (73.96%)	339 (76.35%)	328 (71.30%)	271 (74.45%)		
No	81 (6.39%)	25 (5.63%)	32 (6.96%)	24 (6.59%)		
Reported were able to see a health care provider of a similar race or religion						0.14
Always or most of the time	760 (59.94%)	279 (62.84%)	276 (60.00%)	205 (56.32%)		
Some or none of the time	387 (30.52%)	124 (27.93%)	139 (30.22%)	124 (34.07%)		

Table 2.

Multivariable Ordinal Regression analysis of socioeconomic characteristics and patient-reported barriers to care by disease severity among *All of Us* participants with glaucoma

	OR	95% CI	P values
Age at first glaucoma diagnosis	1.00	0.99 – 1.01	0.75
Sex			
Male	Ref	Ref	Ref
Female	0.94	0.76 – 1.17	0.59
Race			
White	Ref	Ref	Ref
Black/African American	2.20	1.62 – 3.00	< **0.001**
Other	0.77	0.52 – 1.14	0.20
Ethnicity			
Not Hispanic or Latino	Ref	Ref	Ref
Hispanic or Latino	1.65	0.97 – 2.80	0.07
Education			
High school degree/GED or less	Ref	Ref	Ref
Some college	0.92	0.64 – 1.32	0.67
College graduate or advanced degree	1.13	0.81 – 1.57	0.49
Annual Income			
$25,000 or less	Ref	Ref	Ref
$25,000 - $50,000	0.90	0.60 – 1.35	0.61
$50,000 - $100,000	0.89	0.62 – 1.26	0.51
$100,000 - $200,000	0.93	0.62 – 1.40	0.72
$200,000 or more	1.14	0.69 – 1.88	0.61
Insurance			
Medicaid	Ref	Ref	Ref
Medicare	1.12	0.70 – 1.78	0.64
VA/Military	1.16	0.60 – 2.06	0.73
Other insurance	0.92	0.57 – 1.49	0.72
HCAUS Question			
Reported needing eyeglasses but not getting them because they couldn't afford it within the last 12 months	1.04	0.66 – 1.64	0.87
Reported asking doctor for lower cost medication because they couldn't afford it within the last 12 months	1.09	0.83 – 1.44	0.53
Reported not seeing a specialist because they couldn't afford it with in the last 12 months	1.22	0.72 – 2.05	0.46
Reported delaying medical care because they were paying out of pocket for part or all of the procedure within the last 12 months	0.95	0.63 – 1.44	0.81
Reported speaking to an eye doctor within the last 12 months	0.97	0.63 – 1.49	0.88
Reported most or all of the time were able to see a health care provider of a similar race or religion	0.84	0.67 – 1.06	0.14