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Priorities for health outcomes in glaucoma in an ethnically diverse UK cohort: observational study

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Abstract

Objectives: To assess whether patients from minority ethnic groups have different perceptions about the quality of life (QoL) outcomes that matter most to them.

Design: Cross-sectional observational study.

Setting: High volume eye centres serving the most ethnically diverse region in the UK, recruiting from July 2021 to February 2022.

Participants: 511 patients with primary open-angle glaucoma and the pre-disease state of ocular hypertension.

Main outcome measures: The main outcome was participants' self-reported priorities for health outcomes.

Results: Participants fell into one of four clusters with differing priorities for health outcomes, namely: (1) vision, (2) drop-freedom, (3) intraocular pressure (4) one-time treatment. Ethnicity was the strongest determinant of cluster membership after adjusting for potential confounders. Compared to White patients prioritizing vision alone, the odds ratio (OR) for Black/Black British patients was 7.31 [95% confidence interval 3.43–15.57, p<0.001] for prioritizing drop-freedom; 5.95 [2.91–12.16, p<0.001] for intraocular pressure; and 2.99 [1.44–6.18, p=0.003] for one-time treatment. For Asian/Asian British patients the OR was 3.17 [1.12–8.96, p=0.030] for prioritizing intraocular pressure as highly as vision. Other ethnic minority groups also had higher ORs for prioritizing health outcomes other than vision alone: 4.50 [1.03–19.63, p=0.045] for drop freedom and 5.37 [1.47–19.60, p=0.011] for intraocular pressure.

Conclusions: Ethnicity is strongly associated with differing perceptions about the health outcomes that matter. An individualised and ethnically inclusive approach is needed when selecting and evaluating treatments in clinical and research settings.

Strengths and limitations of this study

- This is the first study assessing priorities for health outcomes in a racially diverse cross-section of participants with the common chronic disease of glaucoma.
- To ensure that our findings are not unfairly biased against ethnic minority groups, we recruited from the most ethnically diverse region in the UK so that nearly 50% of the participants were from ethnic minority groups.
- We have adjusted for the confounding effect of socioeconomic status by including individual-level data on education, income and occupation in our logistic model.
- We assessed co-variates captured from routinely collected medical record data across the whole range of disease severity and treatment history, thereby maximising the generalizability of our findings.
- Preference elicitation using Best-Worst Scaling may involve a cognitive burden for respondents which is nonetheless lower than traditional ranking Discrete Choice Experiments.

INTRODUCTION

Important differences in health outcomes by ethnic group are well recognized. In the US, all-cause mortality is substantially higher for the Black ethnic group compared with the White ethnic group across the life span.(1, 2) In England and Wales, ischaemic heart disease mortality is highest in the Bangladeshi, Pakistani and Indian groups.(3) Apart from mortality, wide inequalities in self-reported health-related quality of life (QoL) have been identified between different ethnic groups in the UK. The negative effect on QoL among Bangladeshi, Pakistani, Arab and Gypsy or Irish Traveller ethnic groups is similar to or greater than the impact of being 20 years older in the whole population.(4) To address ethnic inequalities in health outcomes, it is important to understand the underlying reasons.(5, 6)

Differences in socioeconomic position, access to care, and healthcare experience may be partly accountable.(7-9) But even after controlling for social and economic disadvantage, differences in health still exist.(10-12) Beyond social determinants, possible explanations for disparities in health outcomes by ethnic group include differential susceptibility to disease and differential responses to treatment. These issues are exemplified by glaucoma, a chronic disease that is the leading cause of irreversible blindness and accounts for approximately 80% of blindness globally.(13, 14) For Black patients compared to White patients, glaucoma is more prevalent, develops 10 years earlier on average, and is 15 times more likely to cause visual impairment.(15-17) The outcomes of medical and surgical treatment for glaucoma are worse for Black than White populations.(18, 19) However, the idea that health risks are inevitably associated with particular ethnic groups or genetic profiles is being challenged. Conveying race as a disease risk factor without context may be a form of structural racism that perpetuates stereotypes of some groups as more diseased than others.(6, 20, 21) Diagnostic and treatment algorithms or guidelines that inappropriately take ethnicity into consideration may lead to unsuitable treatment, exacerbating disparities.(6, 20, 21) Thus, there is a pressing need to better understand why health outcomes are worse in minority ethnic groups.(4)

Minority ethnic and other underrepresented groups affirm that their needs and preferences should be used to improve healthcare delivery and outcomes.(22) Moreover, they find providers and researchers to be unresponsive to their medical needs regarding treatment options. It has been suggested that ethnic groups perceive aspects of their QoL differently because they respond differently to instruments that measure it.(23) Yet, there is scant evidence about whether individual patients have different priorities for health outcomes and, if so, how ethnicity may influence those differing priorities. To address this poverty of health outcome data and help promote equitable healthcare in underserved populations,(24) we now examine this question directly.

METHODS

Study population

Patients who were under treatment at Moorfield's Eye Hospital and St George's University Hospital, United Kingdom were identified and screened from July 2021 to February 2022. These National Health Service (NHS) centres serve the most racially diverse population in the UK, receiving referrals from both community practitioners and secondary care.(25) All participants had to have been diagnosed with open-angle glaucoma or the closely-related condition of ocular hypertension, and to have already experienced treatment (eye drops, laser, or surgery) to lower intraocular pressure. Patients with other ophthalmic pathology were excluded. Participants were required to be able to understand, read and speak English without translation. After informed consent was obtained, participants completed the discrete choice experiment. Self-reported sociodemographic data (gender, ethnicity, income, education, employment status, marital status) were collected by questionnaire. Ethnicity was classified according to ONS categories used in the NHS.(25-27) Although race and ethnicity can be defined separately, they are often used interchangeably. The terms race and ethnicity were used in this article in line with current recommendations.(28, 29) Education, employment and income were classified according to UK Biobank criteria.(30)

Clinical evaluation

To maintain the real-world nature of the data, clinical parameters such as intraocular pressure, visual fields (VF), visual acuity, and medication were obtained during standard clinical care episodes. For the analysis of clinical parameters (listed in Table 1), we set identical timeframes for each patient over the 60 months leading up to the date of recruitment. VF Mean Deviation (MD) was extracted from the Humphrey Field Analyzer 24-2 Swedish Interactive Threshold Algorithm (Carl Zeiss Meditec, Dublin, CA, USA).

The mean MD from the two most recent VFs within an 18-month time window was calculated to estimate disease severity in each eye at the time of recruitment. We chose to take a mean from two VFs to reduce noise in the data owing to expected variability in test performance. However, we limited the analysis window to 18 months to minimize error introduced through true progression of disease.

To estimate disease progression for each eye, the rate of change of MD was calculated by linear regression on all VF conducted during the 60-month timeframe.

Discrete Choice Experiment (DCE)

To elicit individual-level health outcome priorities from participants, we conducted a DCE using Best-Worst Scaling (BWS), a preference elicitation method introduced by Finn and Louviere.(31, 32).

We adopted a "case 1" BWS design in which multiple small subsets of outcomes are shown to patients, who are asked to choose the most important (best) and least important (worst) of the outcomes in each presented subset.(33) Ranking small subsets of outcomes in a BWS design is cognitively straightforward and produces more robust results than being required to consider all outcomes simultaneously. Moreover, BWS delivers a score showing the relative importance of outcomes, not just a rank order. The method only requires an assumption of ordinality.

Our previous work identified outcomes related to disease and treatment that were important to patients who have glaucoma.(34) These outcomes were control of intraocular pressure (eye pressure), maintaining vision, being independent, having a one-time treatment, drop freedom, and having a treatment that does not change. We decided to consider one additional outcome related to treatment, namely avoiding side-effects of eye drops, because this outcome was coded most frequently across the previous study and was thus potentially important. To ensure all seven outcomes were presented an equal number of times, we used a balanced incomplete block design (35) to generate three outcomes in each of 7 sets.

Pilot testing of the DCE with patients was performed to ensure that the instructions were clear. To mitigate the risk of data entry errors, both BWS and sociodemographic data were collected and managed electronically using a secure web-based platform.

Sample size

BWS measures are derived from multinomial frequency counts. Thus, the sample size for this study was calculated based on a multinomial distribution.(36, 37) Under the assumption of the worst possible case in which 3 of the outcomes are selected equally one-third of the time and all other outcomes are never selected, 510 patients were required to ensure that at least 95% of all estimated probabilities of a category being selected are within 0.05 of their true probability.

Statistical analysis

DCE

For each participant, we calculated the BWS score, defined as the number of times an outcome was chosen as the most important (best) minus the number of times an outcome was chosen as the least important (worst) among the presented outcomes.(35) To confirm whether the BWS tasks had been completed appropriately, we checked the relationship between the aggregated most and least counts across the seven outcomes. To assess the consistency of participants' choices, the distribution of individual-level variance was

assessed.(35) In addition, the distribution of individual scores for each outcome was checked. Analyses were performed using R software (version 4.2.1) and IBM SPSS (version 20).

Cluster analysis

To identify participants whose priorities are similar we applied cluster analysis to participants' BWS scores. Cluster analysis is a technique to classify participants into groups (clusters) that are homogenous within themselves and heterogeneous between each other (38, 39). A two-step cluster analysis was chosen as it creates clusters based on categorical and continuous variables and identifies the optimum number of clusters. Satisfactory cluster formation was verified using logistic regression with BWS scores as co-variates.

Multivariate regression model

The association of cluster membership with sociodemographic variables and clinical characteristics was analysed using a multinomial logistic regression model. To control for social and economic disadvantage, we included education, employment and income as individual-level measures of deprivation. Relevant variables related to disease severity and treatment history were selected using clinical judgement then refined using Pearson correlation matrices and variance inflation factors to avoid multicollinearity. We used the MICE package in R to impute missing data to minimize potential bias and conducted a sensitivity analysis using complete case records to verify the result of the primary analysis.

Patient and public involvement

No patients were directly involved in setting the research question, outcome measures, study design, or implementation. No patients were involved in the interpretation or writing up of results. Researchers involved in the study will disseminate the results to patients and the public through relevant websites and conferences at the national level.

RESULTS

Patients' characteristics

Five hundred and eleven patients agreed to participate, representing over 95% of those eligible and invited to take part (Figure 1). Approximately half of the participants were white (273/511 [53.4%]), and 55.4% (283/511) were male. Overall, participants had a mean (±SD) age of 67.6 (12.4) years, with a mean duration from diagnosis ("living with glaucoma") of 8.5 (7.3) years. Patients had a wide range of disease severities and treatment histories. Sociodemographic and clinical characteristics of the participants are reported in Table 1.

DCE

All participants completed the DCE, with no missing data. To check the performance of the DCE, we conducted several tests. As shown in Figure 2A, aggregate best and worst counts were inversely related, confirming that the DCE was performing appropriately across all participants. Individuals' response consistencies were also checked. Most participants exhibited high score variance (Figure 2B) confirming that most participants gave consistent responses.

Figure 2C shows the distribution of BWS scores from participants for each of the seven outcomes. Scores range from a maximum of +3 to a minimum of -3. Positive scores indicate that the outcome is more important whereas negative scores indicate that the outcome is considered to be less important. A score of +3 indicates that the participant always selected the outcome as being most important whereas a BWS score of -3 indicates that the participant always selected the outcome as being least important. Several distributions are non-normal, which suggests that the underlying responses are heterogeneous, and that cluster analysis is warranted.

Cluster analysis

Figure 3 shows that participants form four large clusters with different priorities for health outcomes. In verification of satisfactory cluster formation,

the deviance statistic shows that the model is a good fit to the data (p = 1.000). That is, individual participants' BWS scores accurately predict cluster membership.

Cluster 1 (vision): This cluster of participants (n=181; 35.4%) assigned the highest priority to the outcome of vision (median BWS score +3).

Cluster 2 (drop freedom): Participants in this cluster (n=98; 19.2%) rated the treatment-related outcome of drop freedom as most important (median BWS score +2).

Cluster 3 (intraocular pressure and vision): The third cluster of participants (n=129; 25.2%) assigned highest priority jointly to intraocular pressure and vision (median BWS score +2).

Cluster 4 (one-time treatment and vision): The final cluster (n=103; 20.2%) prioritized one-time treatment and vision equally (median BWS score +2).

Multivariate regression model

To determine which variables were associated with each cluster we used a multivariate logistic regression model that included all sociodemographic and clinical co-variates stated in Table 1.

Independent predictors of each cluster and their corresponding odds ratios (ORs) and 95% confidence intervals (CI) are shown in Table 2. Cluster 1 (vision) was chosen as the reference cluster. The proportion of missing values was 0.9% and occurred only for data on income and in the records used to obtain disease and treatment data. There were no missing data on self-reported ethnicity or other sociodemographic variables. We conducted a sensitivity analysis to determine whether missing data impacted our analysis. Complete case analysis did not alter our conclusions compared to use of the multiply imputed dataset.

The most striking finding is that ethnicity was a strong predictor of membership across clusters and thus of health outcome priorities. Ethnicity was the sole significant co-variate for cluster 4 (one-time treatment and vision), and the major co-variate for cluster 2 (drop freedom).

Cluster 2 (drop freedom): The odds of patients with Black/Black British ethnicity and other ethnic groups belonging to cluster 2 were 7.31 [95% CI, 3.43–15.57] and 4.50 [95% CI, 1.03–19.63] times higher, respectively, than white patients. They were much more likely than their white counterparts to choose drop freedom ahead of vision. The duration for which patients had been living with glaucoma had a modest influence on membership of this cluster, with each additional year decreasing the odds by a factor of 0.94 (95% CI, 0.90–0.99). This suggests that patients may become slightly more accepting of eye drops with time.

Cluster 3 (intraocular pressure and vision): ORs associating ethnicity with membership of this cluster were 5.95 [95% CI, 2.91–12.16] for Black/Black British, 3.17 [95% CI, 1.12 – 8.96] for Asian/Asian British and 5.37 [95% CI, 1.47–19.60] for Other ethnic groups. These patients were much more likely than their white counterparts to assign equal priority to intraocular pressure and vision. For patients with an average annual income of £52,000 – £100,000, the OR was 0.07 [95% CI, 0.02 – 0.28], which means that those with this income had 93% lower odds of jointly prioritizing intraocular pressure and vision than those with the lowest incomes (<£18,000). Apart from these sociodemographic factors, patients' treatment history significantly affected the discrimination between cluster 3 and cluster 1. Patients who had received laser treatment had 3.94 [95% CI, 1.17 – 13.29] times higher odds of regarding intraocular pressure to be as important as vision compared to those who had needed eye drops only.

Cluster 4 (one-time treatment and vision): Ethnicity was the only co-variate that was significantly associated with this cluster. The OR for prioritizing one-time treatment as highly as vision was 2.99 [95% CI, 1.44 – 6.18] for Black/Black British patients.

DISCUSSION

In this discrete choice experiment, we found that patients with glaucoma have different priorities for the outcomes of their care. We identified major racial and ethnic disparities in personal priorities, showing for the first time that minority ethnic groups may have differing expectations of the outcomes of care compared to their White counterparts. These differences need to be considered if racial disparities in health outcomes are to be understood and hence equitably addressed.

Collecting data on ethnic groups is complex because of the subjective, multifaceted and changing nature of ethnic identification. It has been pointed out that there is no consensus on what constitutes an ethnic group and membership is something that is self-defined and subjectively meaningful to the person concerned.(40) We used contemporaneously self-reported information on ethnicity, in line with recent recommendations.(41)

Information about ethnic inequalities in health is limited by paucity of data from underrepresented populations.(42) To ensure that our findings are not unfairly biased against ethnic minority groups, we recruited from the most ethnically diverse region in the UK so that nearly 50% of the participants were from ethnic minority groups.(25) We note that large population-based samples such as UK Biobank underrepresent individuals with socioeconomic deprivation and from particular ethnic backgrounds, demonstrating that studies of large scale do not necessarily avoid data disparities in which there are systematic differences in the quantity and quality of health data representing different ethnic groups.(43)

Ethnic disparities in health outcomes may reflect inequalities between ethnic groups in terms of socioeconomic position.(7) We have adjusted for the confounding effect of socioeconomic status by including individual-level data on education, income and occupation in our logistic model. We have also corrected for age, gender, disease status and treatment history.

We used real-world data from the patient population. In contrast to prospective trials or case series, we assessed co-variates captured from

routinely collected medical record data across the whole range of disease severity and treatment history. This maximises the generalizability of our findings to patients routinely seen in glaucoma clinics.

We minimized selection bias by successfully recruiting over 95% of those who were eligible and invited to participate. Our DCE and ethnicity data were complete. Overall only 0.9% of data were missing, and complete case analysis did not alter our conclusions compared to use of the multiply imputed dataset.

Preference elicitation using BWS was completed by patients based on their judgment and understanding of hypothetical descriptions. This may involve a cognitive burden for respondents. However, the burden in BWS is lower than traditional ranking DCEs because it is relatively easy to identify the best and worst items of a list.(44) Patients were asked to make choices between health priorities, all of which had been identified as important in a previous study.(34) Despite the risk of ambivalence, choice consistency as measured by variance was excellent (Figure 2B), suggesting that most patients were clear about what really mattered most to them.

Our findings are consistent with those from previous studies in which intraocular pressure was identified as an important goal in glaucoma management.(45, 46) Whereas it was previously reported that intraocular pressure was the top priority for all patients,(47) we found that other outcomes were prioritized by different groups of patients. There may be several explanations for the apparent discrepancy. First, Le et al enrolled predominately White patients which may have prevented them from detecting ethnic disparities in preferences. Second, they examined only the aggregated preferences of the whole cohort, and therefore did not check whether there were clusters of individuals with differing priorities. Third, they enrolled patients with early disease who were supposedly suitable for minimally-invasive glaucoma surgery, thus limiting elicited preferences to this rather specific group. By contrast, we recruited patients across the broad spectrum of glaucoma severity with varied treatment histories.

The present findings have several important implications. First, patients' health outcome priorities may not necessarily coincide with their clinicians' assumptions. This challenges the recent proposal that vision should be the primary outcome in all clinical trials of glaucoma treatment.(48) A significant proportion of patients in our study prioritized drop-freedom most highly, implying that evaluation of glaucoma treatments should take a bespoke approach, taking each patient's priorities into account. This supports previous suggestions that patients should define for themselves those aspects of health that impact on QoL, not just in glaucoma but in a variety of clinical settings.(49-51) Alternatively, clinicians and researchers would need to use measures of QoL that are validated as being sensitive across the gamut of differing patient priorities. Interestingly, minimally-invasive glaucoma surgical procedures have been suggested as a new therapeutic option for glaucoma patients who wish to reduce their medication.(52, 53) However, evidence that drop-freedom is a desired outcome from the patients' perspective was previously lacking. Our study shows that a significant proportion of patients, but not all, do value drop-freedom.

Secondly, certain treatments may be more suitable for some ethnic groups than others. It was much more likely that Black and certain other ethnic groups prized drop-freedom as the most important health outcome. The Black ethnic group was also more likely to prioritize one-time treatment as highly as vision. Overall, this suggests that these groups would be more likely to benefit from drop-freedom produced by one-off treatments such as selective laser trabeculoplasty and minimally-invasive glaucoma surgery.(52-54) It also helps to explain previous reports that patients from Black ethnic groups were less likely to use their glaucoma eye-drop medications regularly.(55) Thus identifying patient preferences is important when considering treatment options to maximize concordance with treatment and optimize outcomes, especially in patients with aggressive disease. We speculate that similar disparities in outcome preference may explain ethnic differences in treatment compliance in other areas of medicine.(56)

Thirdly, our findings suggest that ethnic groups tend to define aspects of their QoL differently. QoL is a multidimensional concept that encompasses

opportunity, health perceptions, functional status, impairment and life expectancy.(57) Differential priorities for health outcomes may thus explain unexpected dissimilarities found in QoL across ethnic groups in patients with cancer.(23) Notwithstanding suggestions that existing ways of measuring QoL are insufficiently sensitive,(48, 58) the aggregation of the QoL outcomes across different ethnic groups may have masked positive effects of treatment in recent trials.(54, 59) Furthermore, QoL outcomes from studies which predominantly recruit certain ethnic groups may not be generalizable to other ethnic groups.

It is unknown whether ethnic disparities in priorities for health outcomes exist in other specialisms of healthcare. Regarding the ethnic contrasts demonstrated here, it will be important to determine whether they differ in other geographic regions such that clinicians will need to be aware of the peculiarities of the populations they serve. Longitudinal studies will be required to assess whether individual preferences are stable with time. The reasons underlying the ethnic disparities reported here need further investigation. We cannot exclude the possibility that these disparities may themselves originate in psychological, behavioural and physiological responses of individuals to racism and discrimination.(21)

Legends (Tables and Figures):

Table 1. Sociodemographic and Clinical Characteristics of Patients Included in the Study

Table 2. Association of clusters with significant predictors

Figure 1. Flowchart. Number of individuals at each stage of the study.

Figure 2. A. Graph of Most (x) versus 1/(least) (y) for aggregate BWS scores for each of the seven outcomes (dots). B. Histograms of variances (VAR) estimated from individual BWS scores. C. Histograms of individual BWS scores

Figure 3. Cluster analysis of health outcome priorities.

Ethical approval: Approval for the study was granted by the North West – Haydock Research Ethics Committee (REC reference 20/N.W./0347).

Data availability statement: The data that support the findings of this study are not openly available to avoid compromising individual privacy. However anonymised data are available from the corresponding author upon reasonable request.

Contributors: All authors have made substantive intellectual contributions; AS performed the study design, data collection, data analysis, and manuscript preparation. KH performed the study design, data interpretation, and manuscript preparation. EK performed data interpretation and manuscript critique. GG performed study design and manuscript critique. KH and GG had supervisory roles and oversaw administrative and financial aspects. KH is the study guarantor. The corresponding author attests that all listed authors meet authorship criteria and that no others meeting the criteria have been omitted.

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The lead author (KH) affirms that this manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned have been explained.

Dissemination to participants and related patient and public communities: This work was presented at the Royal College of Ophthalmologists Annual Congress 2023.

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TABLES

Table 1. Sociodemographic and Clinical Characteristics of Patients Included in the Study

Characteristics	All patients (n = 511)
Gender, n (%)	
Female	228 (44.6)
Male	283 (55.4)
Age, years, range, mean (SD)	26 – 92, 67.6 (12.4)
Ethnicity†	
White	273 (53.4)
Black/Black British	154 (30.1)
Asian/Asian British	49 (9.6)
Mixed	11 (2.2)
Others	24 (4.7)
Marital status, n (%)	
Widowed	54 (10.6)
Married	305 (59.7)
Civil partnered, including separated	18 (3.5)
Divorced	51 (10.0)
Single	83 (16.2)
Education, n (%)	
College	215 (42.1)
A level	42 (8.2)
O level	61 (11.9)
CSE	21 (4.1)
NVQ	40 (7.8)
Other professional qualifications	65 (12.7)
None of the above	67 (13.1)
Employment, n (%)	
In-paid employment	173 (33.9)
Retired	295 (57.7)
Looking after home	11 (2.2)
Unable to work due to sickness	8 (1.6)
None of the above	5 (1.0)
Doing unpaid	5 (1.0)
Full-time/part-time student	7 (1.4)
Unemployed	7 (1.4)
Income‡, n (%)	
< £18.000	233 (45.6)
£18.000 – £30.999	129 (25.2)
£31.000 – £51.999	83 (16.2)
£52.000 – £100.000	46 (9.0)
> £100.000	20 (3.9)
Duration of living with glaucoma, years, range, mean (SD)	0.1 – 34.7, 8.5 (7.3)
Current intraocular pressure, mmHg, range, mean (SD)	
Better eye	4 – 49, 17.33 (5.29)
Worse eye	2 – 44, 17.06 (6.19)
Current MD, dB, range, mean (SD)*	
Better eye	-28.5 – 3.59, -3.94 (5.94)
Worse eye	-33.5 – 2.14, -9.19 (8.16)
MD change rate, dB/year, range, mean (SD)**	
Better eye	-1.29 – 2.09, 0.0 (0.24)
Worse eye	-0.77 – 1.45, -0.02 (1.8)
Visual acuity baseline, logMAR mean (SD)	
Better eye	-0.3 – 2.4, 0.15 (0.36)
Worse eye	-0.3– 2.4, 0.2 (0.32)
Glaucoma medication, range, mean (SD)	
No of glaucoma medication used by patient (current)††	0 - 4, 1.32 (0.98)
No of instillations (current)^	0 - 8, 2.67 (2.19)
Medication Escalation over previous 18 months¶	-3 - 17, 0.62 (1.89)
Medication Escalation over previous 5 years‖	-4 - 19, 1.61 (2.63)
Laser procedures, median (range)	
No of SLT per patient	0 (0 – 5)
Surgery procedures, median (range)	
No of surgery per patient	0 (0 – 5)
Most recent surgical procedure, n (%)	
Nil	335 (65.6)
Trabeculectomy	69 (13.5)
Shunt	18 (3.5)
MIGS	26 (5.1)
Other glaucoma procedures	4 (0.8)
Phacoemulsification	59 (11.5)

Maximum glaucoma therapy§, better eye, n (%)	
Surgery	104 (20.4)
Laser	101 (19.8)
Drops	306 (59.9)
Maximum glaucoma therapy§, worse eye, n (%)	
Surgery	146 (28.6)
Laser	108 (21.1)
Drops	257 (50.3)

†Ethnicity as per National Health Service categories: White (British, Irish, any other white background), Black or Black British (Caribbean, African, another Black background), Asian or Asian British (Indian, Pakistani, Bangladeshi, any other Asian background), Mixed (White and Black Caribbean, White and Black African, White and Asian, any other mixed background), Other ethnic groups including Chinese
‡Average total household income before tax (£) based on Biobank
***Calculated as mean from the two most recent visual field tests within 18 months prior to recruitment**
****Calculated using linear regression of all visual field tests within 60 months prior to recruitment**
††No of glaucoma medication is number of drugs used by patient
^Sum total of drop preparations used for each eye
¶Cumulative number of drug escalations over 18 months prior to recruitment
|||Cumulative number of drug escalations over 5 years prior to recruitment
§Maximum glaucoma therapy is defined by invasiveness. Drops were considered to be the least invasive treatment and glaucoma surgery of any kind was considered to be the most invasive.
LogMAR, logarithm of the minimum angle of resolution; MD, mean deviation; SD, standard deviation; SLT, Selective laser trabeculoplasty

Table 2. Association of clusters with significant predictors

Cluster§	Parameter	P value	Odds Ratio	95% Confidence Interval	
				Lower Bound	Upper Bound
2 (drop freedom)	**Ethnicity**				
	Black or Black British	<.001	7.31	3.43	15.57
	Other ethnic groups	0.045	4.50	1.03	19.63
	White*				
	Living with disease (years)	0.017	0.94	0.90	0.99
3 (intraocular pressure and vision)	**Ethnicity**				
	Asian or Asian British	0.030	3.17	1.12	8.96
	Black or Black British	<.001	5.95	2.91	12.16
	Other ethnic groups	0.011	5.37	1.47	19.60
	White*				
	Income				
	£52,000 – £100,000	<.001	0.07	0.02	0.28
	£ <18,000*				
	Maximum glaucoma therapy, worse eye				
	Laser	0.027	3.94	1.17	13.29
	Drops*				
4 (one-time treatment and vision)	**Ethnicity**				
	Black or Black British	0.003	2.99	1.44	6.18
	White*				

§**The reference cluster** is: 1 (vision).
*__Reference group__

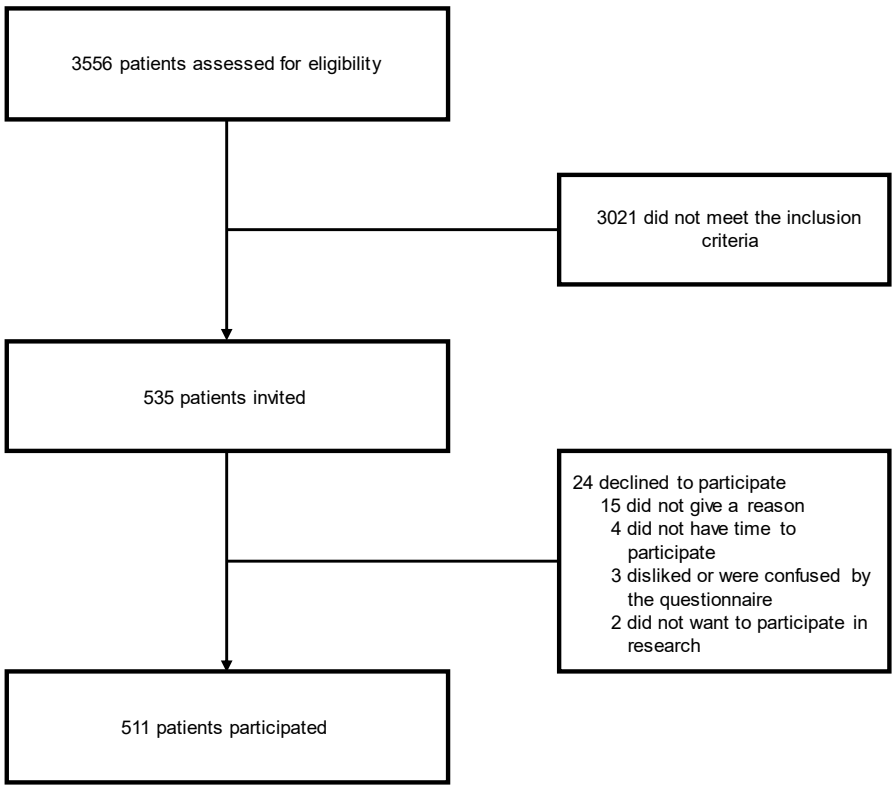

Figure 1. Flowchart. Number of individuals at each stage of the study.

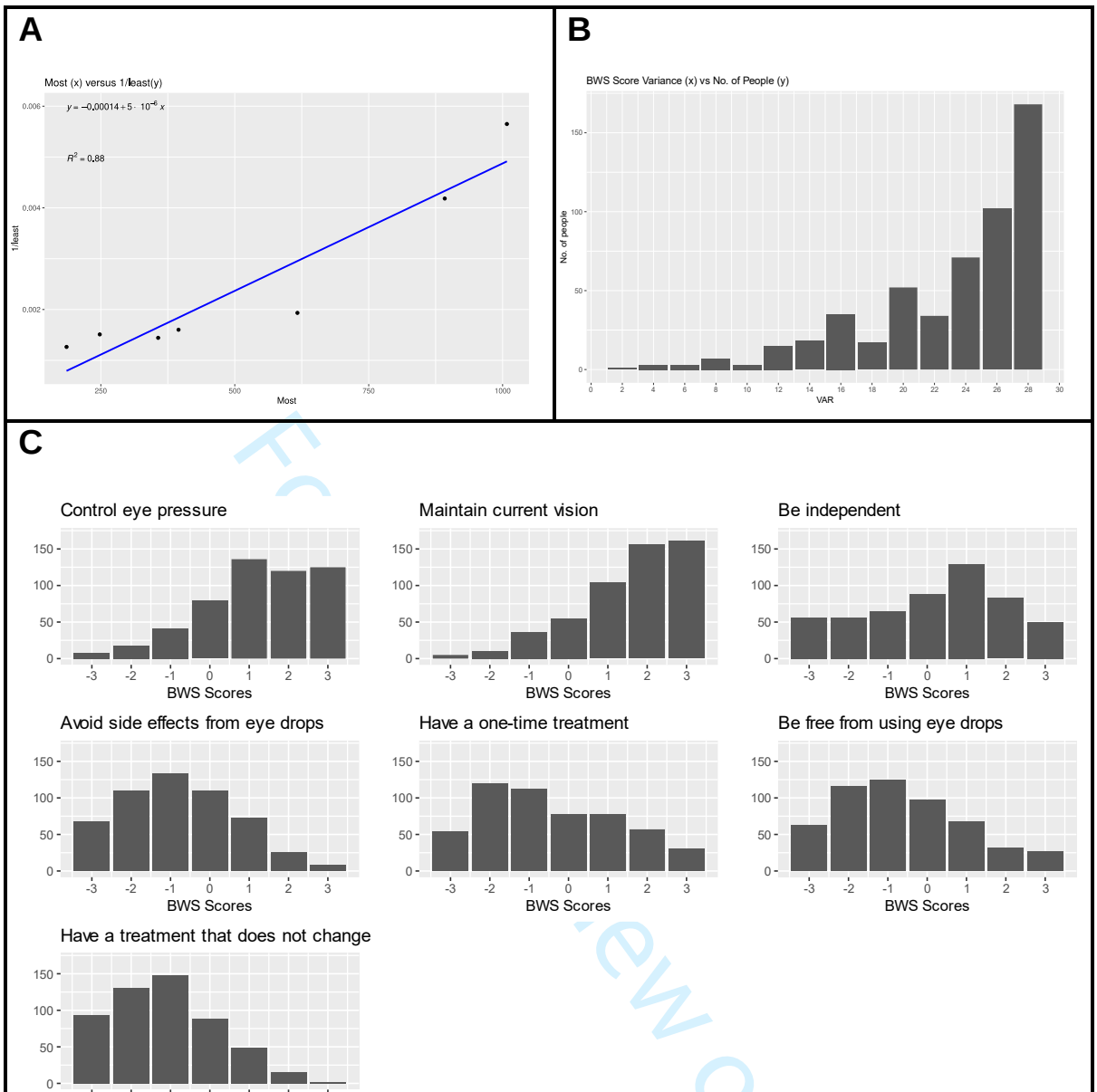

Figure 2. A. Graph of Most (x) versus 1/(least) (y) for aggregate BWS scores for each of the seven outcomes (dots). The graph is consistent with most and least counts being inversely related (blue linear regression line). **B. Histograms of variances (VAR) estimated from individual BWS scores.** Higher values on the variance scale mean more choice consistency, with lower values meaning less consistency. **C. Histograms of individual BWS scores.** These suggest heterogeneous responses, confirming the need to perform cluster analysis.

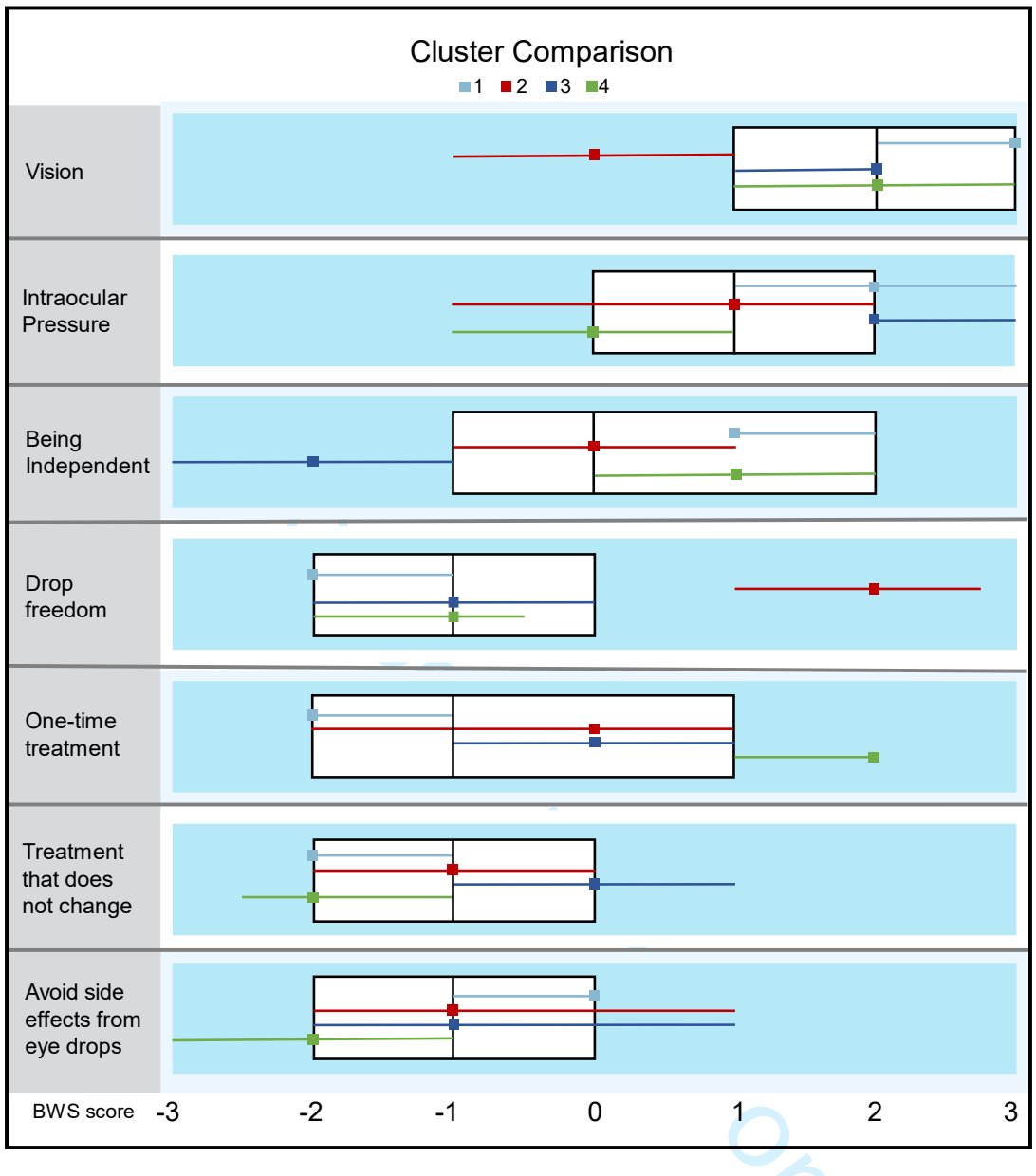

Figure 3. Cluster analysis of health outcome priorities. Four clusters with different priorities for health outcomes are formed by participants according to their BWS scores. The highest ranked health priority for each cluster is as follows: vision (Cluster 1, light blue), drop-freedom (Cluster 2, red), intraocular pressure and vision (Cluster 3, dark blue), one-time treatment and vision (Cluster 4, green). BWS scores for each outcome are shown segregated by cluster. More positive scores indicate more important outcomes, whereas more negative scores indicate less important outcomes. For reference, scores for the entire cohort are presented in the white boxplot. Medians are represented by dots (for clusters) and by vertical lines (for entire cohort). Interquartile range is shown by whiskers (for clusters) and box (for entire cohort).

STROBE Statement—Checklist of items that should be included in reports of ***cross-sectional studies***

	Item No	Recommendation	Page No
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	3
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4-5
Objectives	3	State specific objectives, including any prespecified hypotheses	5
Methods			
Study design	4	Present key elements of study design early in the paper	6
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5-6
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants	5
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	5-6,8
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	*5-6*
Bias	9	Describe any efforts to address potential sources of bias	8
Study size	10	Explain how the study size was arrived at	7
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	7-8
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	7-8
		(*b*) Describe any methods used to examine subgroups and interactions	8
		(*c*) Explain how missing data were addressed	8
		(*d*) If applicable, describe analytical methods taking account of sampling strategy	N/A
		(*e*) Describe any sensitivity analyses	8
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	9
		(b) Give reasons for non-participation at each stage	9
		(c) Consider use of a flow diagram	9
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	9
		(b) Indicate number of participants with missing data for each variable of interest	9
Outcome data	15*	Report numbers of outcome events or summary measures	10
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	10-11

		(*b*) Report category boundaries when continuous variables were categorized	10-11
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	N/A
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	9-10
Discussion			
Key results	18	Summarise key results with reference to study objectives	12
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	12-13
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	13-15
Generalisability	21	Discuss the generalisability (external validity) of the study results	14-15
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	16-17

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

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Priorities for health outcomes in glaucoma in an ethnically diverse UK cohort: observational study

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Priorities for health outcomes in glaucoma in an ethnically diverse UK cohort: observational study

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Word count: 3547

Subject areas: Ophthalmology

Abstract

Objectives: To assess whether patients from minority ethnic groups have different perceptions about the quality of life (QoL) outcomes that matter most to them.

Design: Cross-sectional observational study.

Setting: High volume eye centres serving the most ethnically diverse region in the UK, recruiting from July 2021 to February 2022.

Participants: 511 patients with primary open-angle glaucoma and the pre-disease state of ocular hypertension.

Main outcome measures: The main outcome was participants' self-reported priorities for health outcomes.

Results: Participants fell into one of four clusters with differing priorities for health outcomes, namely: (1) vision, (2) drop-freedom, (3) intraocular pressure (4) one-time treatment. Ethnicity was the strongest determinant of cluster membership after adjusting for potential confounders. Compared to White patients prioritizing vision alone, the odds ratio (OR) for Black/Black British patients was 7.31 [95% confidence interval 3.43–15.57, p<0.001] for prioritizing drop-freedom; 5.95 [2.91–12.16, p<0.001] for intraocular pressure; and 2.99 [1.44–6.18, p=0.003] for one-time treatment. For Asian/Asian British patients the OR was 3.17 [1.12–8.96, p=0.030] for prioritizing intraocular pressure as highly as vision. Other ethnic minority groups also had higher ORs for prioritizing health outcomes other than vision alone: 4.50 [1.03–19.63, p=0.045] for drop freedom and 5.37 [1.47–19.60, p=0.011] for intraocular pressure.

Conclusions: Ethnicity is strongly associated with differing perceptions about the health outcomes that matter. An individualised and ethnically inclusive approach is needed when selecting and evaluating treatments in clinical and research settings.

Strengths and limitations of this study

- To ensure that our findings are not unfairly biased against ethnic minority groups, we recruited from the most ethnically diverse region in the UK so that nearly 50% of the participants were from ethnic minority groups.
- We have adjusted for the confounding effect of socioeconomic status by including individual-level data on education, income and occupation in our logistic model.
- We assessed co-variates captured from routinely collected medical record data across the whole range of disease severity and treatment history, thereby maximising the generalizability of our findings.
- Preference elicitation using Best-Worst Scaling may involve a cognitive burden for respondents.
- It may have been difficult for some participants to choose between health priorities that were all considered to be important.

INTRODUCTION

Important differences in health outcomes by ethnic group are well recognized. In the US, all-cause mortality is substantially higher for the Black ethnic group compared with the White ethnic group across the life span.(1, 2) In England and Wales, ischaemic heart disease mortality is highest in the Bangladeshi, Pakistani and Indian groups.(3) Apart from mortality, wide inequalities in self-reported health-related quality of life (QoL) have been identified between different ethnic groups in the UK. The negative effect on QoL among Bangladeshi, Pakistani, Arab and Gypsy or Irish Traveller ethnic groups is similar to or greater than the impact of being 20 years older in the whole population.(4) To address ethnic inequalities in health outcomes, it is important to understand the underlying reasons.(5, 6)

Differences in socioeconomic position, access to care, and healthcare experience may be partly accountable.(7-9) But even after controlling for social and economic disadvantage, differences in health still exist.(10-12) Beyond social determinants, possible explanations for disparities in health outcomes by ethnic group include differential susceptibility to disease and differential responses to treatment. These issues are exemplified by glaucoma, a chronic disease that is the leading cause of irreversible blindness and accounts for approximately 80% of blindness globally.(13, 14) For Black patients compared to White patients, glaucoma is more prevalent, develops 10 years earlier on average, and is 15 times more likely to cause visual impairment.(15-17) The outcomes of medical and surgical treatment for glaucoma are worse for Black than White populations.(18, 19) However, the idea that health risks are inevitably associated with particular ethnic groups or genetic profiles is being challenged. Conveying race as a disease risk factor without context may be a form of structural racism that perpetuates stereotypes of some groups as more diseased than others.(6, 20, 21) Diagnostic and treatment algorithms or guidelines that inappropriately take ethnicity into consideration may lead to unsuitable treatment, exacerbating disparities.(6, 20, 21) Thus, there is a pressing need to better understand why health outcomes are worse in minority ethnic groups.(4)

Minority ethnic and other underrepresented groups affirm that their needs and preferences should be used to improve healthcare delivery and outcomes.(22) Moreover, they find providers and researchers to be unresponsive to their medical needs regarding treatment options. It has been suggested that ethnic groups perceive aspects of their QoL differently because they respond differently to instruments that measure it.(23) Yet, there is scant evidence about whether individual patients have different priorities for health outcomes and, if so, how ethnicity may influence those differing priorities. To address this poverty of health outcome data and help promote equitable healthcare in underserved populations,(24) we now examine this question directly.

METHODS

Study population

Patients who were under treatment at Moorfield's Eye Hospital and St George's University Hospital, United Kingdom were identified and screened from July 2021 to February 2022. These National Health Service (NHS) centres serve the most racially diverse population in the UK, receiving referrals from both community practitioners and secondary care.(25) All participants had to have been diagnosed with open-angle glaucoma or the closely-related condition of ocular hypertension, and to have already experienced treatment (eye drops, laser, or surgery) to lower intraocular pressure. Patients with other ophthalmic pathology were excluded. Participants were required to be able to understand, read and speak English without translation. After written informed consent was obtained, participants completed the discrete choice experiment. Self-reported sociodemographic data (gender, ethnicity, income, education, employment status, marital status) were collected by questionnaire. Ethnicity was classified according to ONS categories used in the NHS.(25-27) Although race and ethnicity can be defined separately, they are often used interchangeably. The terms race and ethnicity were used in this article in line with current recommendations.(28, 29) Education, employment and income were classified according to UK Biobank criteria.(30)

Clinical evaluation

To maintain the real-world nature of the data, clinical parameters such as intraocular pressure, visual fields (VF), visual acuity, and medication were obtained during standard clinical care episodes. For the analysis of clinical parameters (listed in Table 1), we set identical timeframes for each patient over the 60 months leading up to the date of recruitment. VF Mean Deviation (MD) was extracted from the Humphrey Field Analyzer 24-2 Swedish Interactive Threshold Algorithm (Carl Zeiss Meditec, Dublin, CA, USA).

The mean MD from the two most recent VFs within an 18-month time window was calculated to estimate disease severity in each eye at the time of recruitment. We chose to take a mean from two VFs to reduce noise in the data owing to expected variability in test performance. However, we limited the analysis window to 18 months to minimize error introduced through true progression of disease.

To estimate disease progression for each eye, the rate of change of MD was calculated by linear regression on all VF conducted during the 60-month timeframe.

Table 1. Sociodemographic and Clinical Characteristics of Patients Included in the Study

Characteristics	All patients (n = 511)
Gender, n (%)	
Female	228 (44.6)
Male	283 (55.4)
Age, years, range, mean (SD)	26 – 92, 67.6 (12.4)
Ethnicity†	
White	273 (53.4)
Black/Black British	154 (30.1)
Asian/Asian British	49 (9.6)
Mixed	11 (2.2)
Others	24 (4.7)
Marital status, n (%)	
Widowed	54 (10.6)
Married	305 (59.7)
Civil partnered, including separated	18 (3.5)
Divorced	51 (10.0)
Single	83 (16.2)
Education, n (%)	
College	215 (42.1)
A level	42 (8.2)
O level	61 (11.9)
CSE	21 (4.1)
NVQ	40 (7.8)
Other professional qualifications	65 (12.7)
None of the above	67 (13.1)
Employment, n (%)	
In-paid employment	173 (33.9)
Retired	295 (57.7)
Looking after home	11 (2.2)
Unable to work due to sickness	8 (1.6)
Doing unpaid work	5 (1.0)
Full-time/part-time student	7 (1.4)
Unemployed	7 (1.4)
None of the above	5 (1.0)
Income‡, n (%)	
< £18.000	233 (45.6)
£18.000 – £30.999	129 (25.2)
£31.000 – £51.999	83 (16.2)
£52.000 – £100.000	46 (9.0)
> £100.000	20 (3.9)
Duration of living with glaucoma, years, range, mean (SD)	0.1 – 34.7, 8.5 (7.3)
Current intraocular pressure, mmHg, range, mean (SD)	
Better eye	4 – 49, 17.33 (5.29)
Worse eye	2 – 44, 17.06 (6.19)
Current MD, dB, range, mean (SD)*	
Better eye	-28.5 – 3.59, -3.94 (5.94)
Worse eye	-33.5 – 2.14, -9.19 (8.16)
MD change rate, dB/year, range, mean (SD)**	
Better eye	-1.29 – 2.09, 0.0 (0.24)
Worse eye	-0.77 – 1.45, -0.02 (1.8)
Visual acuity baseline, logMAR mean (SD)	
Better eye	-0.3 – 2.4, 0.15 (0.36)
Worse eye	-0.3– 2.4, 0.2 (0.32)
Glaucoma medication, range, mean (SD)	
No of glaucoma medication used by patient (current)††	0 - 4, 1.32 (0.98)
No of instillations (current)^	0 - 8, 2.67 (2.19)
Medication Escalation over previous 18 months¶	-3 - 17, 0.62 (1.89)
Medication Escalation over previous 5 years|||	-4 - 19, 1.61 (2.63)
Laser procedures, median (range)	
No of SLT per patient	0 (0 – 5)
Surgery procedures, median (range)	
No of surgery per patient	0 (0 – 5)
Most recent surgical procedure, n (%)	
Nil	335 (65.6)
Trabeculectomy	69 (13.5)
Shunt	18 (3.5)
MIGS	26 (5.1)
Other glaucoma procedures	4 (0.8)
Phacoemulsification	59 (11.5)

Maximum glaucoma therapy§, better eye, n (%)	
Surgery	104 (20.4)
Laser	101 (19.8)
Drops	306 (59.9)
Maximum glaucoma therapy§, worse eye, n (%)	
Surgery	146 (28.6)
Laser	108 (21.1)
Drops	257 (50.3)

†Ethnicity as per National Health Service categories: White (British, Irish, any other white background), Black or Black British (Caribbean, African, another Black background), Asian or Asian British (Indian, Pakistani, Bangladeshi, any other Asian background), Mixed (White and Black Caribbean, White and Black African, White and Asian, any other mixed background), Other ethnic groups including Chinese
‡Average total household income before tax (£) based on UK Biobank
***Calculated as mean from the two most recent visual field tests within 18 months prior to recruitment**
****Calculated using linear regression of all visual field tests within 60 months prior to recruitment**
††No of glaucoma medication is number of drugs used by patient
^Sum total of drop preparations used for each eye
¶Cumulative number of drug escalations over 18 months prior to recruitment
|||Cumulative number of drug escalations over 5 years prior to recruitment
§Maximum glaucoma therapy is defined by invasiveness. Drops were considered to be the least invasive treatment and glaucoma surgery of any kind was considered to be the most invasive.
LogMAR, logarithm of the minimum angle of resolution; MD, mean deviation; MIGS, minimally invasive glaucoma surgery; SD, standard deviation; SLT, selective laser trabeculoplasty

Discrete Choice Experiment (DCE)

To elicit individual-level health outcome priorities from participants, we conducted a DCE using Best-Worst Scaling (BWS), a preference elicitation method introduced by Finn and Louviere.(31, 32).

We adopted a "case 1" BWS design in which multiple small subsets of outcomes are shown to patients, who are asked to choose the most important (best) and least important (worst) of the outcomes in each presented subset.(33) Ranking small subsets of outcomes in a BWS design is cognitively straightforward and produces more robust results than being required to consider all outcomes simultaneously. Moreover, BWS delivers a score showing the relative importance of outcomes, not just a rank order. The method only requires an assumption of ordinality.

Our previous work identified outcomes related to disease and treatment that were important to patients who have glaucoma.(34) These outcomes were control of intraocular pressure (eye pressure), maintaining vision, being independent, having a one-time treatment, drop freedom, and having a treatment that does not change. We decided to consider one additional outcome related to treatment, namely avoiding side-effects of eye drops, because this outcome was coded most frequently across the previous study and was thus potentially important. To ensure all seven outcomes were presented an equal number of times, we used a balanced incomplete block design (35) to generate three outcomes in each of 7 sets.

Pilot testing of the DCE with patients was performed to ensure that the instructions were clear. Both BWS and sociodemographic data were collected in person from participants in the hospital setting immediately following recruitment. To mitigate the risk of data entry errors, responses were keyed directly into a secure web-based platform and managed electronically.

Sample size

BWS measures are derived from multinomial frequency counts. Thus, the sample size for this study was calculated based on a multinomial distribution.(36, 37) Under the assumption of the worst possible case in which 3 of the outcomes are selected equally one-third of the time and all other outcomes are never selected, 510 patients were required to ensure that at least 95% of all estimated probabilities of a category being selected are within 0.05 of their true probability.

Statistical analysis

DCE

For each participant, we calculated the BWS score, defined as the number of times an outcome was chosen as the most important (best) minus the number of times an outcome was chosen as the least important (worst) among the presented outcomes.(35) To confirm whether the BWS tasks had been completed appropriately, we checked the relationship between the aggregated most and least counts across the seven outcomes. To assess the consistency of participants' choices, the distribution of individual-level variance was assessed.(35) In addition, the distribution of individual scores for each outcome was checked. Analyses were performed using R software (version 4.2.1) and IBM SPSS (version 20).

Cluster analysis

To identify participants whose priorities are similar we applied cluster analysis to participants' BWS scores. Cluster analysis is a technique to classify participants into groups (clusters) that are homogenous within themselves and heterogeneous between each other (38, 39). A two-step cluster analysis was chosen as it creates clusters based on categorical and continuous variables and identifies the optimum number of clusters. Satisfactory cluster formation was verified using logistic regression with BWS scores as co-variates.

Multivariate regression model

The association of cluster membership with sociodemographic variables and clinical characteristics was analysed using a multinomial logistic regression model. To control for social and economic disadvantage, we included education, employment and income as individual-level measures of deprivation. Relevant variables related to disease severity and treatment history were selected using clinical judgement then refined using Pearson correlation matrices and variance inflation factors to avoid multicollinearity. We used the MICE package in R to impute missing data to minimize potential bias and conducted a sensitivity analysis using complete case records to verify the result of the primary analysis.

Patient and public involvement

No patients were directly involved in setting the research question, outcome measures, study design, or implementation. No patients were involved in the interpretation or writing up of results. Researchers involved in the study will disseminate the results to patients and the public through relevant websites and conferences at the national level.

RESULTS

Patients' characteristics

Five hundred and eleven patients agreed to participate, representing over 95% of those eligible and invited to take part (Figure 1). Approximately half of the participants were white (273/511 [53.4%]), and 55.4% (283/511) were male. Overall, participants had a mean (±SD) age of 67.6 (12.4) years, with a mean duration from diagnosis ("living with glaucoma") of 8.5 (7.3) years. Patients had a wide range of disease severities and treatment histories. Sociodemographic and clinical characteristics of the participants are reported in Table 1.

DCE

All participants completed the DCE, with no missing data. To check the performance of the DCE, we conducted several tests. As shown in Figure 2A, aggregate best and worst counts were inversely related, confirming that the

DCE was performing appropriately across all participants. Individuals' response consistencies were also checked. Most participants exhibited high score variance (Figure 2B) confirming that most participants gave consistent responses.

Figure 2C shows the distribution of BWS scores from participants for each of the seven outcomes. Scores range from a maximum of +3 to a minimum of -3. Positive scores indicate that the outcome is more important whereas negative scores indicate that the outcome is considered to be less important. A score of +3 indicates that the participant always selected the outcome as being most important whereas a BWS score of -3 indicates that the participant always selected the outcome as being least important. Several distributions are non-normal, which suggests that the underlying responses are heterogeneous, and that cluster analysis is warranted.

Cluster analysis

Figure 3 shows that participants form four large clusters with different priorities for health outcomes. In verification of satisfactory cluster formation, the deviance statistic shows that the model is a good fit to the data (p = 1.000). That is, individual participants' BWS scores accurately predict cluster membership.

Cluster 1 (vision): This cluster of participants (n=181; 35.4%) assigned the highest priority to the outcome of vision (median BWS score +3).

Cluster 2 (drop freedom): Participants in this cluster (n=98; 19.2%) rated the treatment-related outcome of drop freedom as most important (median BWS score +2).

Cluster 3 (intraocular pressure and vision): The third cluster of participants (n=129; 25.2%) assigned highest priority jointly to intraocular pressure and vision (median BWS score +2).

Cluster 4 (one-time treatment and vision): The final cluster (n=103; 20.2%) prioritized one-time treatment and vision equally (median BWS score +2).

Multivariate regression model

To determine which variables were associated with each cluster we used a multivariate logistic regression model that included all sociodemographic and clinical co-variates stated in Table 1.

Independent predictors of each cluster and their corresponding odds ratios (ORs) and 95% confidence intervals (CI) are shown in Table 2. Cluster 1 (vision) was chosen as the reference cluster. The proportion of missing values was 0.9% and occurred only for data on income and in the records used to obtain disease and treatment data. There were no missing data on self-reported ethnicity or other sociodemographic variables. We conducted a sensitivity analysis to determine whether missing data impacted our analysis. Complete case analysis did not alter our conclusions compared to use of the multiply imputed dataset.

The most striking finding is that ethnicity was a strong predictor of membership across clusters and thus of health outcome priorities. Ethnicity was the sole significant co-variate for cluster 4 (one-time treatment and vision), and the major co-variate for cluster 2 (drop freedom).

Cluster 2 (drop freedom): The odds of patients with Black/Black British ethnicity and other ethnic groups belonging to cluster 2 were 7.31 [95% CI, 3.43–15.57] and 4.50 [95% CI, 1.03–19.63] times higher, respectively, than white patients. They were much more likely than their white counterparts to choose drop freedom ahead of vision. The duration for which patients had been living with glaucoma had a modest influence on membership of this cluster, with each additional year decreasing the odds by a factor of 0.94 (95% CI, 0.90–0.99). This suggests that patients may become slightly more accepting of eye drops with time.

Cluster 3 (intraocular pressure and vision): ORs associating ethnicity with membership of this cluster were 5.95 [95% CI, 2.91–12.16] for Black/Black British, 3.17 [95% CI, 1.12 – 8.96] for Asian/Asian British and 5.37 [95% CI, 1.47–19.60] for Other ethnic groups. These patients were much more likely than their white counterparts to assign equal priority to intraocular pressure and vision. For patients with an average annual income of £52,000 – £100,000, the OR was 0.07 [95% CI, 0.02 – 0.28], which means that those with this income had 93% lower odds of jointly prioritizing intraocular pressure and vision than those with the lowest incomes (<£18,000). Apart from these sociodemographic factors, patients' treatment history significantly affected the discrimination between cluster 3 and cluster 1. Patients who had received laser treatment had 3.94 [95% CI, 1.17 – 13.29] times higher odds of regarding intraocular pressure to be as important as vision compared to those who had needed eye drops only.

Cluster 4 (one-time treatment and vision): Ethnicity was the only co-variate that was significantly associated with this cluster. The OR for prioritizing one-time treatment as highly as vision was 2.99 [95% CI, 1.44 – 6.18] for Black/Black British patients.

Table 2. Association of clusters with significant predictors

Cluster§	Parameter	P value	Odds Ratio	95% Confidence Interval	
				Lower Bound	Upper Bound
2 (drop freedom)	**Ethnicity**				
	Black or Black British	<.001	7.31	3.43	15.57
	Other ethnic groups	0.045	4.50	1.03	19.63
	White*				
	Living with disease (years)	0.017	0.94	0.90	0.99
3 (intraocular pressure and vision)	**Ethnicity**				
	Asian or Asian British	0.030	3.17	1.12	8.96
	Black or Black British	<.001	5.95	2.91	12.16
	Other ethnic groups	0.011	5.37	1.47	19.60
	White*				
	Income				
	£52,000 – £100,000	<.001	0.07	0.02	0.28
	£ <18,000*				
	Maximum glaucoma therapy, worse eye				
	Laser	0.027	3.94	1.17	13.29
	Drops*				
4 (one-time treatment and vision)	**Ethnicity**				
	Black or Black British	0.003	2.99	1.44	6.18
	White*				

§The reference cluster is: 1 (vision).
***Reference group**

DISCUSSION

In this discrete choice experiment, we found that patients with glaucoma have different priorities for the outcomes of their care. We identified major racial and ethnic disparities in personal priorities, showing for the first time that minority ethnic groups may have differing expectations of the outcomes of care compared to their White counterparts. These differences need to be considered if racial disparities in health outcomes are to be understood and hence equitably addressed.

Collecting data on ethnic groups is complex because of the subjective, multifaceted and changing nature of ethnic identification. It has been pointed out that there is no consensus on what constitutes an ethnic group and membership is something that is self-defined and subjectively meaningful to the person concerned.(40) We used contemporaneously self-reported information on ethnicity, in line with recent recommendations.(41)

Information about ethnic inequalities in health is limited by paucity of data from underrepresented populations.(42) To ensure that our findings are not unfairly biased against ethnic minority groups, we recruited from the most ethnically diverse region in the UK so that nearly 50% of the participants were from ethnic minority groups.(25) We note that large population-based samples such as UK Biobank underrepresent individuals with socioeconomic deprivation and from particular ethnic backgrounds, demonstrating that studies of large scale do not necessarily avoid data disparities in which there are systematic differences in the quantity and quality of health data representing different ethnic groups.(43)

Ethnic disparities in health outcomes may reflect inequalities between ethnic groups in terms of socioeconomic position.(7) We have adjusted for the confounding effect of socioeconomic status by including individual-level data on education, income and occupation in our logistic model. We have also corrected for age, gender, disease status and treatment history.

We used real-world data from the patient population. In contrast to prospective trials or case series, we assessed co-variates captured from routinely collected medical record data across the whole range of disease severity and treatment history. This maximises the generalizability of our findings to patients routinely seen in glaucoma clinics.

We minimized selection bias by successfully recruiting over 95% of those who were eligible and invited to participate. Our DCE and ethnicity data were complete. Overall only 0.9% of data were missing, and complete case analysis did not alter our conclusions compared to use of the multiply imputed dataset.

There are limitations in the present analyses. First, preference elicitation using BWS was completed by patients based on their judgment and understanding of hypothetical descriptions. This may involve a cognitive burden for respondents. However, the burden in BWS is lower than traditional ranking DCEs because it is relatively easy to identify the best and worst items of a list.(44) Secondly, patients were asked to make choices between health priorities, all of which had been identified as important in a previous study.(34) It may have been difficult for some patients to choose between these priorities because of ambivalence. However, choice consistency as measured by variance was excellent (Figure 2B), suggesting that the majority of patients were clear about what really mattered most to them. A third limitation is that we used some retrospectively collected data from medical records and we did not double-check with participants whether the data were correct.

Our findings are consistent with those from previous studies in which intraocular pressure was identified as an important goal in glaucoma management.(45, 46) Whereas it was previously reported that intraocular pressure was the top priority for all patients,(47) we found that other outcomes were prioritized by different groups of patients. There may be several explanations for the apparent discrepancy. First, Le et al enrolled predominately White patients which may have prevented them from detecting ethnic disparities in preferences. Second, they examined only the aggregated preferences of the whole cohort, and therefore did not check whether there were clusters of individuals with differing priorities. Third, they enrolled patients

with early disease who were supposedly suitable for minimally-invasive glaucoma surgery, thus limiting elicited preferences to this rather specific group. By contrast, we recruited patients across the broad spectrum of glaucoma severity with varied treatment histories.

The present findings have several important implications. First, patients' health outcome priorities may not necessarily coincide with their clinicians' assumptions. This challenges the recent proposal that vision should be the primary outcome in all clinical trials of glaucoma treatment.(48) A significant proportion of patients in our study prioritized drop-freedom most highly, implying that evaluation of glaucoma treatments should take a bespoke approach, taking each patient's priorities into account. This supports previous suggestions that patients should define for themselves those aspects of health that impact on QoL, not just in glaucoma but in a variety of clinical settings.(49-51) Alternatively, clinicians and researchers would need to use measures of QoL that are validated as being sensitive across the gamut of differing patient priorities. Interestingly, minimally-invasive glaucoma surgical procedures have been suggested as a new therapeutic option for glaucoma patients who wish to reduce their medication.(52, 53) However, evidence that drop-freedom is a desired outcome from the patients' perspective was previously lacking. Our study shows that a significant proportion of patients, but not all, do value drop-freedom.

Secondly, certain treatments may be more suitable for some ethnic groups than others. It was much more likely that Black and certain other ethnic groups prized drop-freedom as the most important health outcome. The Black ethnic group was also more likely to prioritize one-time treatment as highly as vision. Overall, this suggests that these groups would be more likely to benefit from drop-freedom produced by one-off treatments such as selective laser trabeculoplasty and minimally-invasive glaucoma surgery.(52-54) It also helps to explain previous reports that patients from Black ethnic groups were less likely to use their glaucoma eye-drop medications regularly.(55) Thus identifying patient preferences is important when considering treatment options to maximize concordance with treatment and optimize outcomes, especially in patients with aggressive disease. We speculate that similar

disparities in outcome preference may explain ethnic differences in treatment compliance in other areas of medicine.(56)

Thirdly, our findings suggest that ethnic groups tend to define aspects of their QoL differently. QoL is a multidimensional concept that encompasses opportunity, health perceptions, functional status, impairment and life expectancy.(57) Differential priorities for health outcomes may thus explain unexpected dissimilarities found in QoL across ethnic groups in patients with cancer.(23) Notwithstanding suggestions that existing ways of measuring QoL are insufficiently sensitive,(48, 58) the aggregation of the QoL outcomes across different ethnic groups may have masked positive effects of treatment in recent trials.(54, 59) Furthermore, QoL outcomes from studies which predominantly recruit certain ethnic groups may not be generalizable to other ethnic groups.

It is unknown whether ethnic disparities in priorities for health outcomes exist in other specialisms of healthcare. Regarding the ethnic contrasts demonstrated here, it will be important to determine whether they differ in other geographic regions such that clinicians will need to be aware of the peculiarities of the populations they serve. Longitudinal studies will be required to assess whether individual preferences are stable with time. The reasons underlying the ethnic disparities reported here need further investigation. We cannot exclude the possibility that these disparities may themselves originate in psychological, behavioural and physiological responses of individuals to racism and discrimination.(21)

Legends (Tables and Figures):

Table 1. Sociodemographic and Clinical Characteristics of Patients Included in the Study

Table 2. Association of clusters with significant predictors

Figure 1. Flowchart. Number of individuals at each stage of the study.

Figure 2. A. Graph of Most (x) versus 1/(least) (y) for aggregate BWS scores for each of the seven outcomes (dots). The graph is consistent with most and least counts being inversely related (blue linear regression line). **B. Histograms of variances (VAR) estimated from individual BWS scores.** Higher values on the variance scale mean more choice consistency, with lower values meaning less consistency. **C. Histograms of individual BWS scores.** These suggest heterogeneous responses, confirming the need to perform cluster analysis.

Figure 3. Cluster analysis of health outcome priorities. Four clusters with different priorities for health outcomes are formed by participants according to their BWS scores. The highest ranked health priority for each cluster is as follows: vision (Cluster 1, light blue), drop-freedom (Cluster 2, red), intraocular pressure and vision (Cluster 3, dark blue), one-time treatment and vision (Cluster 4, green). BWS scores for each outcome are shown segregated by cluster. More positive scores indicate more important outcomes, whereas more negative scores indicate less important outcomes. For reference, scores for the entire cohort are presented in the white boxplot. Medians are represented by dots (for clusters) and by vertical lines (for entire cohort). Interquartile range is shown by whiskers (for clusters) and box (for entire cohort).

Ethical approval: Approval for the study was granted by the North West – Haydock Research Ethics Committee (REC reference 20/N.W./0347).

Data availability statement: The data that support the findings of this study are not openly available to avoid compromising individual privacy. However

anonymised data are available from the corresponding author upon reasonable request.

Contributors: All authors have made substantive intellectual contributions; AS performed the study design, data collection, data analysis, and manuscript preparation. KH performed the study design, data interpretation, and manuscript preparation. EK performed data interpretation and manuscript critique. GG performed study design and manuscript critique. KH and GG had supervisory roles and oversaw administrative and financial aspects. KH is the study guarantor. The corresponding author attests that all listed authors meet authorship criteria and that no others meeting the criteria have been omitted.

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The lead author (KH) affirms that this manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned have been explained.

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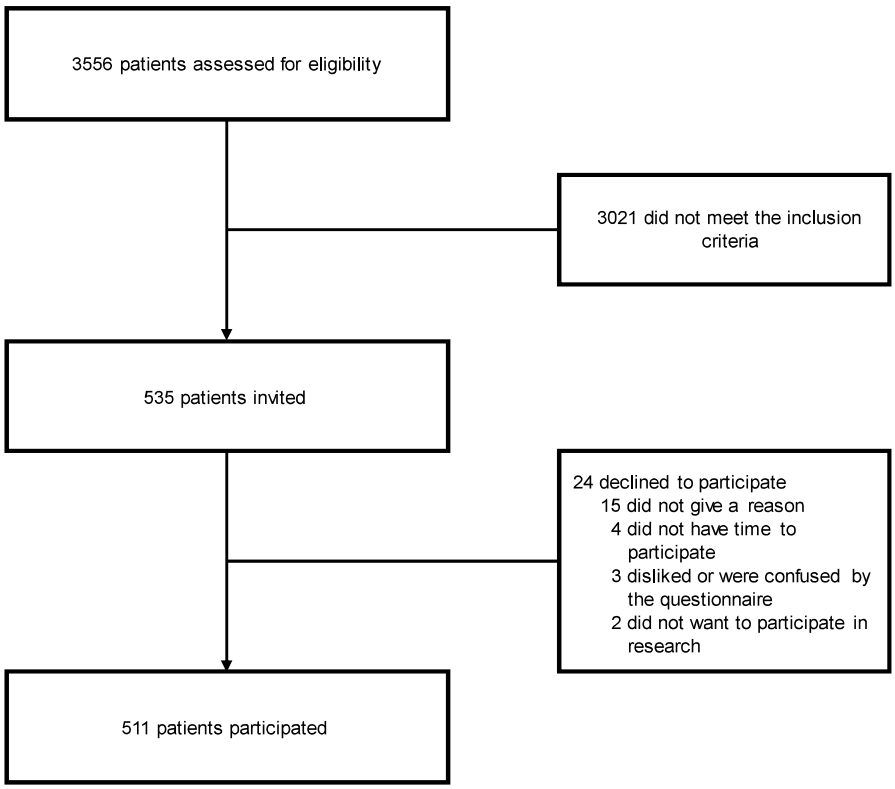

Figure 1. Flowchart. Number of individuals at each stage of the study.

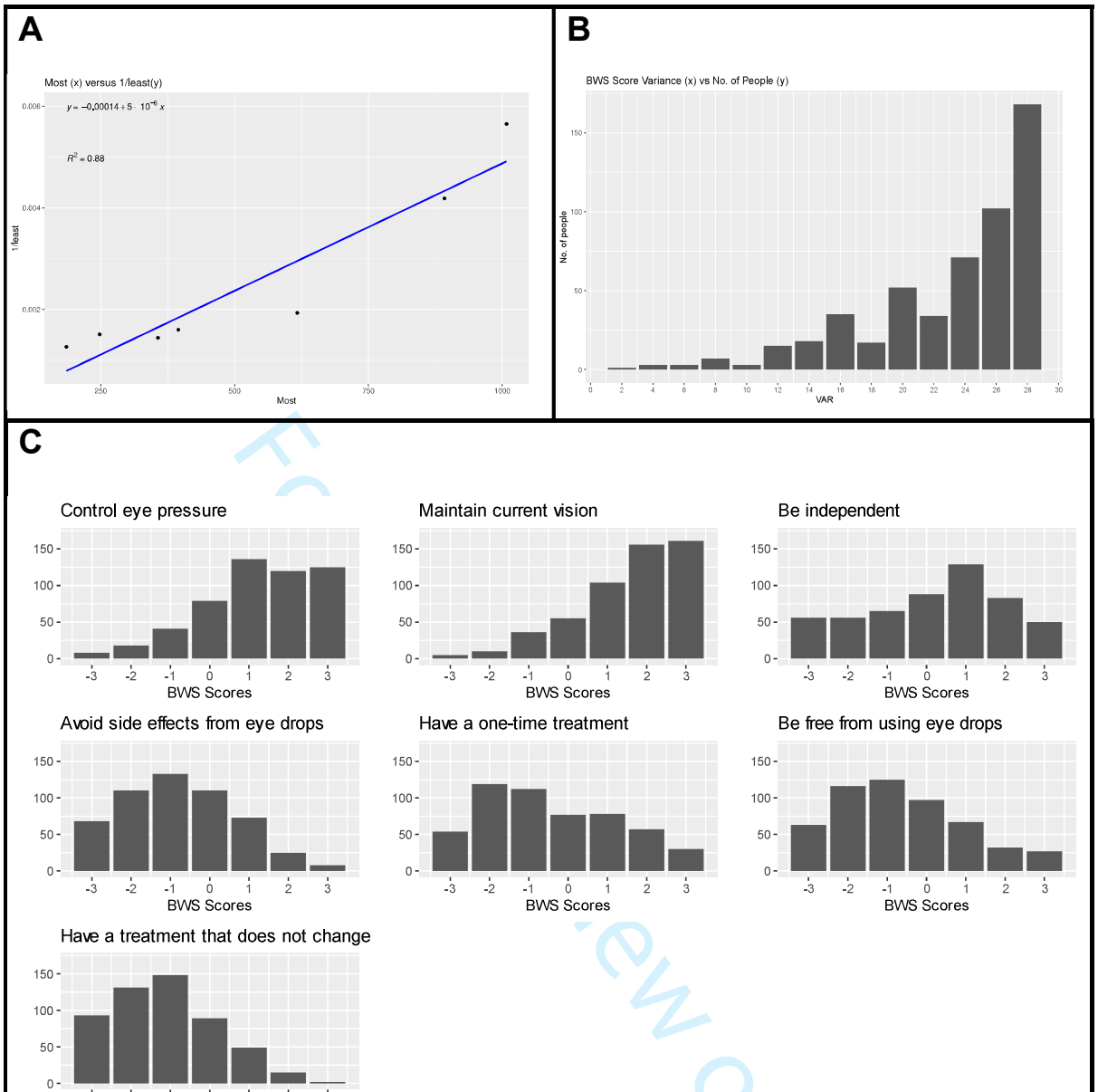

Figure 2. A. Graph of Most (x) versus 1/(least) (y) for aggregate BWS scores for each of the seven outcomes (dots). The graph is consistent with most and least counts being inversely related (blue linear regression line). **B. Histograms of variances (VAR) estimated from individual BWS scores.** Higher values on the variance scale mean more choice consistency, with lower values meaning less consistency. **C. Histograms of individual BWS scores.** These suggest heterogeneous responses, confirming the need to perform cluster analysis.

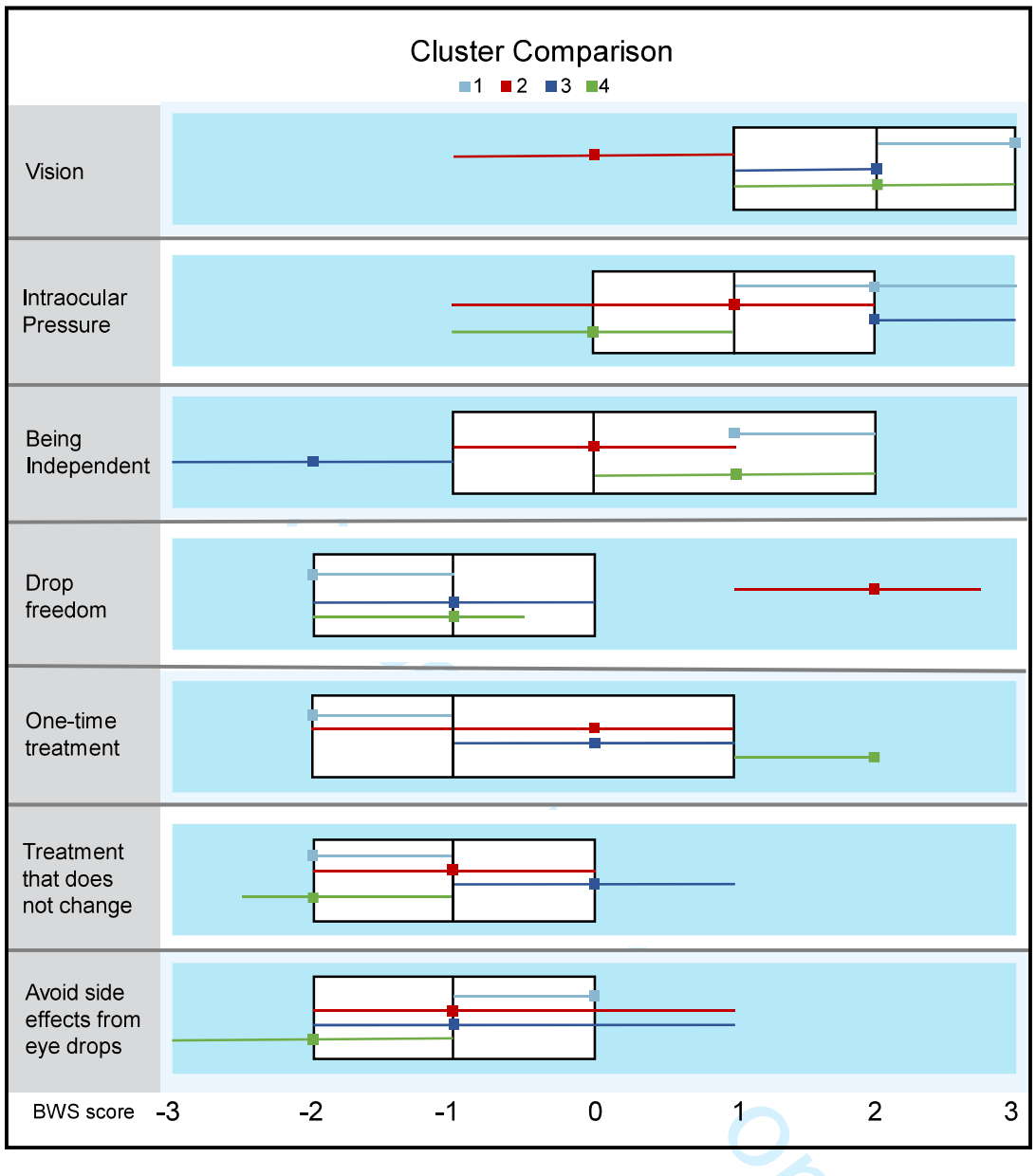

Figure 3. Cluster analysis of health outcome priorities. Four clusters with different priorities for health outcomes are formed by participants according to their BWS scores. The highest ranked health priority for each cluster is as follows: vision (Cluster 1, light blue), drop-freedom (Cluster 2, red), intraocular pressure and vision (Cluster 3, dark blue), one-time treatment and vision (Cluster 4, green). BWS scores for each outcome are shown segregated by cluster. More positive scores indicate more important outcomes, whereas more negative scores indicate less important outcomes. For reference, scores for the entire cohort are presented in the white boxplot. Medians are represented by dots (for clusters) and by vertical lines (for entire cohort). Interquartile range is shown by whiskers (for clusters) and box (for entire cohort).

STROBE Statement—Checklist of items that should be included in reports of ***cross-sectional studies***

	Item No	Recommendation	Page No
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4-5
Objectives	3	State specific objectives, including any prespecified hypotheses	5
Methods			
Study design	4	Present key elements of study design early in the paper	5-11
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants	5
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	6-9
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	5-9
Bias	9	Describe any efforts to address potential sources of bias	5-9
Study size	10	Explain how the study size was arrived at	10
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	6-9
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	10-11
		(*b*) Describe any methods used to examine subgroups and interactions	10-11
		(*c*) Explain how missing data were addressed	11
		(*d*) If applicable, describe analytical methods taking account of sampling strategy	N/A
		(*e*) Describe any sensitivity analyses	11
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	11

		(b) Give reasons for non-participation at each stage	11
		(c) Consider use of a flow diagram	11
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	7-8
		(b) Indicate number of participants with missing data for each variable of interest	11
Outcome data	15*	Report numbers of outcome events or summary measures	12
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	13-15
		(*b*) Report category boundaries when continuous variables were categorized	N/A
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	N/A
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	13-15
Discussion			
Key results	18	Summarise key results with reference to study objectives	16
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	17
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	18-19
Generalisability	21	Discuss the generalisability (external validity) of the study results	16-17
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	21

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.