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ORIGINAL ARTICLE

Developing a Preference-Based Glaucoma Utility Index Using a Discrete Choice Experiment

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ABSTRACT

Purpose. To estimate a utility-based glaucoma health outcome measure, known as the Glaucoma Utility Index.

Methods. Based on focus group studies, involving people with glaucoma, existing profile measures relevant to glaucoma were modified and a six-dimensional profile instrument was developed. Dimensions were: central and near vision; lighting and glare; mobility; activities of daily living; eye discomfort and other effects. Each dimension was assigned four levels (no difficulty; some difficulty; quite a lot of difficulty; and severe difficulty). The discrete choice experiment (DCE) approach was employed to move from this profile instrument to a preference-based utility measure. Experimental design techniques were used to derive a sample of health states for which preferences were elicited using the DCE. Four hundred and seventy-three people with glaucoma received the choice questionnaire.

Results. The regression analysis was based on 286 consistent responses to the DCE. The regression coefficients for three of the dimensions ("central and near vision," "mobility," and "activities of daily living") moved as expected. Moving from "no difficulty" to "severe difficulty" for central and near vision resulted in the most loss of utility, followed by activities of daily living and mobility. Systemic ("other effects") and local side effects were considered the least important. Utility weights were related to self-reported glaucoma state. Utility estimates moved in line with generic measures of health outcome.

Conclusions. This study developed a preference-based utility measure (Glaucoma Utility Index) using the DCE approach. The index, estimated on the basis of 286 respondents, demonstrated both theoretical and convergent validity with other generic health outcome measures and measures of glaucoma severity. Further research investigating preferences by clinically defined glaucoma health status is indicated. Methodological research should focus on alternative methods of scaling for use within a generic Quality Adjusted Life Year framework.

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Key Words: preference, utility, quality weights, discrete choice experiment, glaucoma

Glaucoma is a chronic eye disease characterized by progressive damage to the optic nerve and consequent restriction of the field of vision. The condition does not reduce length of life but is associated with impaired health status and health-related quality of life.[1–5] Traditionally, the outcome of glaucoma care has been judged on intraocular pressure reduction and measures of visual function, mainly an assessment of the visual field.[6] Although clinically useful for monitoring progress, such outcomes do not capture the impact of the condition or its treatment on patients' emotional and physical functioning and lifestyle.

Given limited resources for health care, decisions have to be made about the efficient allocation of scarce health care resources. This has led to an increasing interest in the effectiveness and cost-effectiveness of competing interventions. One way to establish effectiveness is to consider the impact of competing interventions on health outcomes. It is now recognized that patient reported outcomes complement objective clinical measures, and are important as a primary outcome for evaluating the effectiveness of alternative interventions.[7] Recognition of this has led to an increase in the use of profile measures of health outcome. Indeed in the area of oph-

thalmology the need for patient reported outcome measures is well recognized[8] and numerous health profile measures (questionnaires) have been developed and are potentially suitable for assessing health outcome in glaucoma.[9,10]

While profile measures provide separate scores across the range of effects identified as important, they do not reflect preferences for the various domains of the measure.[11] This has led to the development of preference-based single index measures. These can be based on health profile measures relevant to the disease being valued, in this case glaucoma. The index approach has been commonly used within the Quality Adjusted Life Year (QALY) paradigm. Here the number of life-years saved from a given intervention is weighted by the quality (utility) of those life years.[12]

Recent guidance suggests that estimates of QALYs should be based on generic health state valuation methods that reflect the values of the whole population, not just those with the condition of interest.[13] However, generic preference-based instruments, such as the EQ-5D,[14] SF-6D (derived from the UK SF-36),[15] or the Health Utilities Index-mark III(HUI-3),[16,17] which define health in terms of several different dimensions (for example, for the EQ-5D the dimensions are mobility, self-care, usual activities, pain or discomfort, and anxiety or depression), may not be sensitive to changes in health status for some conditions.[18,19] It is unclear how well such generic measures reflect the preferences of those with glaucoma for the avoidance of both the symptoms of glaucoma and side effects of treatment. Indeed, Kobelt et al.[20] used the EQ-5D to estimate utility according to different stages of glaucoma and found that although utility decreased with severity of glaucoma, after adjusting for comorbidity the differences were not significant apart from for severe glaucoma. It should be noted that while this finding may be explained by the low sensitivity of EQ-5D to the health changes associated with glaucoma, an alternative explanation is that EQ-5D is sensitive to visual impairment, but the visual impairments found in glaucoma are not significant enough to impact the scores.[a]

Within the QALY paradigm the common approaches to estimate utility weights are standard gamble (SG) and time trade off (TTO).[11] These approaches anchor valuations between full health and death. This may be unrealistic for many chronic diseases where, for example, death is not a likely outcome, as in the case of glaucoma, and people find it difficult to either risk death in a standard gamble or trade of years of life for perfect vision in a TTO experiment. Jampel et al. found only 22% (43 of 183) of participants with glaucoma were willing to trade any life for ideal vision.[21] Further, utility values correlated poorly with the extent of visual field loss.[22] Saw et al. found similar difficulties in trading between perfect vision and death; in a gamble between perfect vision and blindness only 34% of the participants were prepared to risk blindness for perfect vision.[23]

There is clearly a need to develop a utility-based measure of outcome and to estimate health state values in the area of glaucoma. This is what this study set out to do. Given the problems of SG and TTO in this area, discrete choice experiment (DCE) methodology was used. This technique is attribute or dimension-based. Respondents are presented with a number of choices which vary with respect to dimensions, and associated levels, and for each asked which they prefer (or think is worse). Two other studies have used conjoint analysis (a broad category of techniques including DCE), in the area of glaucoma, examining the relative importance to patients of characteristics of living with glaucoma and its treatment.[24,25] However, neither of these derived a preference-based utility measure, though a recent study has done this within the area of social care for the elderly.[26]

In summary this article estimates utilities for various health outcomes resulting from glaucoma. The specific objectives of the article were to (1) develop a profile instrument, with appropriate dimensions and levels, the Glaucoma Profile Instrument (GPI); (2) estimate preference-based quality weights for this instrument, resulting in the Glaucoma Utility Index (GUI) (3) estimate utility according to glaucoma severity, and (4) assess the theoretical and convergent validity of the developed GUI. In the next section we explain the DCE approach, with specific reference to developing the GUI. The results are then presented and discussed. Consideration is given to future areas for research.

METHODS

DCEs have been used widely to elicit values, including market, transport, and environmental economics.[27] The last 15 years have seen an increasing use of the technique in health economics.[28] Although a limited number of published studies have adopted the DCE methodology to estimate values for different health state profiles,[29–31] only one has used the technique to estimate a utility index.[26]

DCEs draw upon Lancaster's economic theory of value[32] and random utility theory.[33,34] Attributes (dimensions) of the commodity being valued are defined and levels thereafter assigned to them. Statistical design theory is then used to draw an independent sample of scenarios (i.e., combinations of attribute levels) from the full factorial set. These are placed into efficient choice sets and subjects asked to express their preferences by choosing within these choice sets. In what follows we describe the DCE technique within the context of developing a utility measure.

There are 5 key stages:

1. Identifying relevant dimensions of the health outcome measure,
2. Assigning levels to these dimensions,
3. Applying statistical design theory to draw an independent sample of health states from the full set of health states for which preferences will be elicited,
4. Presenting the choice sets and asking respondents to express their preferences by choosing within these choice sets, and
5. Data analysis using regression techniques to establish the utility weights for the different levels of dimensions, and hence overall utility scores for different health states.

Stage 1 and 2: Identifying Dimensions and Associated Levels of the GPI

Qualitative research methods were used, involving people with glaucoma in two focus groups, to establish the content of the profile instrument. In the first stage of this qualitative component, potentially relevant items, dimensions and levels of difficulty were

[a]We thank an anonymous referee for making this point.

identified from existing vision and glaucoma specific quality of life instruments and studies reporting on disability and quality of life in glaucoma,[5,21,35–40] and additionally from expert opinion. These were collated and were used to define the framework of the focus group discussions.

Subjects were recruited from two ophthalmology centers in the United Kingdom (Aberdeen and Leeds). We purposely sampled from hospital-based glaucoma clinics to recruit male and female patients with different stages of disease, different ethnicity, and different ages. The inclusion criteria were people with glaucoma as a main diagnosis, i.e., without other significant eye disease, thus excluding patients who had age-related macular degeneration and cataract as the main cause of visual impairment. Thirty people were invited to attend two separate focus groups, 17 agreed to participate, 9 in the group in Scotland (Aberdeen), and 8 in the group in England (Leeds). An experienced qualitative researcher led both focus groups and explored the participant's views on the areas we had collated concerning the effects of glaucoma on vision, mobility, role performance, mood, and any adverse effects of treatment. Additionally, descriptions of the factors important to patients and levels of difficulty in these key areas were developed. The discussions were audio-taped, and subsequently transcribed and analyzed using framework methodology to identify key areas that were meaningful to patients for inclusion in the glaucoma profile measure.[41]

The key areas reflecting health status were near vision tasks, treatment effects both in and around the eye and effects on general health, illumination, mobility, and visual judgement for activities of daily living. A large number of factors within these key areas of health status were identified, and these were reduced to broader dimensions for incorporation in the DCE. Given DCEs assumes respondents consider all dimensions and trade across them, such studies generally do not have more than six or seven dimensions.[42] Table 1 shows the final dimensions and levels. These were used to define respondent's glaucoma-related health status, and are hereafter referred to as the GPI (see Appendix, available online at www.optvissci.com).

Stage 3: Developing the Choice Sets and Questionnaire

As the instrument consisted of six dimensions, each with four levels, there was a total of 4096 possible profiles or health states. A fractional factorial design was used to reduce the 4096 profiles to a more manageable 32 profiles, while still being able to infer utilities for all possible profiles. Foldover techniques were used to derive 32 choices from these 32 profiles, ensuring orthogonality, minimum overlap, and level balance of the design.[27] Using this method a mirror image of the original design is created by systematically changing the levels in each profile i.e., $0 \Rightarrow 1$, $1 \Rightarrow 2$, $2 \Rightarrow 3$, $3 \Rightarrow 0$. Thus, profile 0123 becomes 1230 (0, 1, 2, 3 refers to the levels of difficulty that are used in the questionnaire where 0 is no difficulty, 1 is some difficulty, 2 is quite a lot of difficulty, 3 is severe difficulty). These two profiles are then used to create a choice set, i.e., profile 0123 is compared with 1230.

There is debate about the number of choice questions a respondent will find manageable. Therefore, three different sets of questionnaires were piloted, including 8 and 16 (using a blocked design), and 32 choice questions, respectively. This piloting indicated that respondents were able to handle 32 choices (based on response rates, item response rates, and rationality tests). Thus, the final questionnaire included 32 discrete choices from the experimental design.

In addition to the experimental design choices, two rationality tests were included to ensure respondents were engaging in the exercise and taking it seriously. Sen's expansion and contraction rationality tests were used.[43] To test the expansion property respondents were first asked to choose the worse of two profiles (A or B). This choice was then widened to a choice between three profiles (A, B, or C) in a nonconsecutive question. A person that chose situation B in the first choice question should not choose A in the expanded one to satisfy the expansion property. To tests the contraction property respondents were asked to choose a situation from a set of three alternatives (A, B, or C). This choice was then narrowed to a set of two alternatives (A or B). The test was satisfied if a respondent who chose situation A in the first choice did not choose option B in the reduced choice set. Respondents were excluded from the regression analysis if they failed *both* tests.

In addition to the 32 choices from the experimental design and two rationality tests, two practice questions were included, resulting in the questionnaire including 36 choices. A guide describing each of the dimensions of quality of life and level of difficulty was included with the questionnaire. An example of a choice question is provided in Fig. 1.

In addition to the choices, the questionnaire included the GPI, based on the identified dimensions and levels of difficulty (see Appendix), the EQ-5D, and a Visual Analogue Scale (VAS) to self rate own health. Information was also collected on self-rating of glaucoma severity (mild, moderate, or severe). Information was also collected on whether glaucoma was bilateral, details of previous glaucoma medications, and previous glaucoma surgery.

Stage 4: Subjects, Setting and Ethical Committee Approval

Participants were selected from attendees at four hospital-based clinics and one community-based glaucoma clinic across two eye centers in the United Kingdom. All patients with glaucoma (any type) as the main diagnosis, or ocular hypertension on treatment, with a reliable visual field test in at least one eye and who were willing to complete the questionnaire were eligible. People suspected of glaucoma but not on treatment were excluded. We also recruited volunteers from The International Glaucoma Association (IGA), a patient organization, following an advertisement in the patient newsletter and the IGA website, anybody with self reported glaucoma was eligible. Four hundred and seventy-three people received the questionnaire, 225 from the clinic-based sample and 248 from the self-selected sample from the IGA.

A subsample of patients, participants from Aberdeen underwent an objective assessment of glaucoma severity, based on binocular visual field loss. This subsample was selected on the basis of convenience as visual field analyses from the previous year were easily accessible. There is no universally agreed staging system for glaucoma severity. Therefore, three ophthalmologists (including one of the authors, J.B.) agreed this classification. For this objective assessment the description of binocular visual field loss was adapted

TABLE 1.
Dimensions and levels of the glaucoma profile instrument

Dimension	Level of difficulty	Regression variables
Dimension 1. Central and near vision: A number of activities such as reading, writing, watching TV, sewing, card games, computer work, reading dials on clocks and cookers, etc. The list is not exclusive and applies to activities similar to these.	1. *No difficulty* means that you have no problem with these or similar activities.	X_{11}
	2. *Some difficulty* means you can still see to do these activities if you want to but it is a struggle.	X_{12}
	3. *Quite a lot of difficulty* means that you may not do these activities as much as you used to because it is difficult to see.	X_{13}
	4. *Severe difficulty* means that you have stopped reading; you may not be able to see adequately to sign important documents or do your accounts.	0
Dimension 2. Lighting and glare: Situations where bright lights may dazzle; it may be difficult to adjust from light to dark and vice versa, it may be difficult to see in dim light. The list is not exhaustive and different levels of light may affect individuals in different ways.	1. *No difficulty* means that you adapt to different lighting levels in the same way as you always have.	X_{21}
	2. *Some difficulty* means that bright light is troublesome and it takes longer than normal to adapt to changes in lighting but it doesn't stop any activities.	X_{22}
	3. *Quite a lot of difficulty* means that you struggle with changes in illumination and, for example, you may have had to stop driving at night.	X_{23}
	4. *Severe difficulty* means that you cannot find your way without assistance if the lighting is poor.	0
Dimension 3. Mobility: Situations where because of eyesight one may have problems crossing roads, or walking along busy pavements, or negotiating steps and kerbs, or tripping into low objects for example children in pushchairs and dogs. One may have had to stop driving because of poor vision.	1. *No difficulty* means you have no difficulty in these areas.	X_{31}
	2. *Some difficulty* means you can manage but have to take more care than normal.	X_{32}
	3. *Quite a lot of difficulty* means that you struggle crossing roads, going down steps and along pavements as you feel that you are likely to trip.	X_{33}
	4. *Severe difficulty* means that you need extra assistance to get around in unfamiliar places.	0
Dimension 4. Activities of daily living: Situations where you may have difficulties in seeing adequately to do domestic, DIY or self-care tasks around the home. This may include difficulties pouring liquid into containers (e.g. water into a glass etc), or problems judging shelf height leading to difficulties putting or retrieving objects into/from cupboards, or being unaware of open cupboards doors and similar problems.	1. *No difficulty* means that you have no difficulty in these or similar aspects of daily living.	X_{41}
	2. *Some difficulty* means you can manage but have to take more care than normal.	X_{42}
	3. *Quite a lot of difficulty* means that you miss the cup, can't reliably place items on shelves, you may cut yourself shaving or have problems with some other self-care activity and you have had to find ways of adapting to the difficulties.	X_{43}
	4. *Severe difficulty* means that you can't undertake these tasks and require assistance.	0
Dimension 5. Eye discomfort: One or both eyes may feel gritty, or dry, or irritable, watery, tired, or sore.	1. *No difficulty* means that your eyes are comfortable.	X_{51}
	2. *Some difficulty* means that there is occasional discomfort in one or both eyes that may be relieved by artificial teardrops and it is not particularly bothersome.	X_{52}
	3. *Quite a lot of difficulty* means that one or both eyes feel uncomfortable for most of the time and additional lubricant teardrops help but are required often.	X_{53}
	4. *Severe difficulty* means that one or both eyes are constantly uncomfortable and lubricant drops do not relieve discomfort.	0
Dimension 6. Other effects of glaucoma and its' treatment: Situations where one may feel unduly tired, or may have shortness of breath, or a dry mouth, or an after taste, or may have other effects such as some difficulties with sexual functioning.	1. *No difficulty* means that you have not noticed any such difficulties.	X_{61}
	2. *Some difficulty* means that you may have noticed occasional difficulty in one or more of these areas.	X_{62}
	3. *Quite a lot of difficulty* means that you may feel constantly tired, or you may have noticed that you have become short of breath or you may have noticed other difficulties.	X_{63}
	4. *Severe difficulty* means that you have required or think you require additional treatment to control one or more of these difficulties.	0

Each choice question describes two health state situations: Situation A and B. Imagine that you have these difficulties and pick the scenario you think is **WORSE**. You may not like either situation but choose the one that is less preferable to you by putting a tick in the appropriate box. Please tick just ONE box for every question.

SITUATION A	SITUATION B
No difficulty with: • Central and near vision • Lighting and glare • Mobility **Some difficulty** with: • Activities of daily living • Eye discomfort • Other effects of glaucoma and its treatment	**No difficulty** with: • Central and near vision **Some difficulty** with: • Lighting and glare **Quite a lot of difficulty** with: • Activities of daily living • Other effects of glaucoma and its treatment **Severe difficulty** with: • Mobility • Eye discomfort
(Tick one box only) ☐ **Situation A**	✓ **Situation B**

FIGURE 1.
Example of a choice question. In this case the person answering this question thought that the worse option was: having no difficulty with central and near vision, some difficulty with lighting and glare; quite a lot of difficulty with activities of daily living and other effects of glaucoma and its treatment and severe difficulty with mobility and eye discomfort. This is compared with having no difficulty with central and near vision, lighting and glare and mobility; some difficulty with activities of daily living, eye discomfort, and other effects of glaucoma and its treatment.

TABLE 2.
Definition of glaucoma health states

No glaucomatous impairment	Under observation as suspect glaucoma but not on medication and no glaucoma visual field defect in either eye
Mild glaucoma	On treatment, no binocular visual field loss, unilateral glaucoma visual field defect present
Moderate glaucoma	Up to five missed points (<10 dB) in the binocular central 20 degrees of visual field
Severe glaucoma	Binocular visual field loss below UK driving standard[a]

[a]Six or more adjoining missed points (<10 dB), and any additional separate missed point(s) OR a cluster of 4 or more adjoining missed points (<10 dB); either of which is either wholly or partly within the central 20-degree superior/inferior hemispheric field.

from a scoring system of the integrated visual field, whereby uniocular visual field analyses are integrated into a single binocular field without additional testing.[44,45] The definitions of health states are described in Table 2.

Approval was obtained for each phase of the study from the Central Office of Research Ethics Committees. The research was conducted according to the tenets of the Declaration of Helsinki.

Stage 5: Data Analysis

Provisional analysis looked at responses to the developed GPI. The aim here was to test the validity of this instrument. A priori we would expect people with more severe glaucoma to report higher levels of disability and quality of life on the GPI.

Econometric techniques were used to analyze the DCE responses and to estimate an algorithm such that the quality weights could be estimated for all of the outcomes in the profile instrument. A conditional logistic regression model was used to analyze the response data. The analysis was performed using STATA,[46] with the following equation initially being estimated:

$$QW_{ij} = \sum \alpha_{dl} X_{dl} + e + u$$

where QW_{ij} is the quality weight for outcome state i as valued by individual j, X_{dl} is a vector of dummy variables where d represents the domain from the profile measure and l the level of that domain (both defined in Table 1 i.e., X_{11} central and nervous vision, no difficulty). For any given outcome state X_{d1} equals 1 if the state is defined in that state, and 0 otherwise. Severe difficulty is used as

the base comparator for all dimensions, resulting in 18 explanatory variables (three for each dimension, relative to severe difficulty). Thus, 00000 is the base comparator (with all dimensions at severe difficulty), α represents the parameter weights to be estimated for *quite a lot of difficulty*, *some difficulty*, and *no difficulty* for all dimensions, relative to severe difficulty, e is the unobservable error term because of the differences among observations and u is the error term due to differences among respondents. Given the inclusion of dummy variables this model does not impose an interval scale or ordinality on the relationship between the domains and utility.[26]

Where the conditional logistic regression model provided no evidence of a significant difference between levels for a given dimension, using the Wald test, levels were combined and the model re-estimated. Utility scores were estimated using this final model. The Likelihood ratio test was used to establish whether the level of self-reported disease severity impacted on the model and the Wald test was used to test where any differences existed.

Looking at whether the coefficients moved in the expected direction assessed *theoretical validity*. A priori we expected coefficients to increase with reduced levels of difficulty. To assess the *convergent validity* of the GUI, utility scores generated were compared with those from EQ-5D and the VAS data. *Convergent validity* was also assessed by describing utility scores according to level of glaucoma severity, self-reported, and objectively assessed based on binocular visual field loss in the subsample of participants from Aberdeen.

RESULTS

Two hundred and ninety-three questionnaires were returned (response rate 62%). Characteristics of respondents are shown in Table 3. The age and gender of the respondents and clinical characteristics were broadly similar across the three recruitment sites, except that the majority of the volunteer respondents from the patient organization reported that they had open angle glaucoma, whereas over 80% of respondents recruited from the eye centers were unaware of the type of glaucoma they had.

Two hundred and seventy-seven (95%) respondents completed the GPI. Fig. 2 shows the responses for all respondents, and according to self-reported glaucoma severity (263 respondents provided a self assessment of the level of severity of their glaucoma). As glaucoma severity increased respondents report higher levels of

TABLE 3.
Demographic and clinical characteristics of the respondents

Characteristic[a]	Total (n = 293)	IGA (n = 185)	Aberdeen (n = 72)	Leeds (n = 36)
Mean age (year ± SD)	69.7 (10.9)	69.6 (11.1)	70.0 (10.9)	70.3 (10.4)
Female, n(%)	144 (52.2)	95 (53.4)	33 (50)	16 (50)
Type of glaucoma n(%)				
Open angle	123 (46.6)	111 (64.9)	7 (10.9)	5 (15.6)
Closed angle	8 (3)	7 (4.1)	1 (1.6)	
Other	12 (4.5)	9 (5.3)	3 (4.7)	
Don't know	124 (46.4)	44 (25.7)	53 (82.8)	27 (84.4)
Glaucoma n(%)				
Mild	101 (37)	52 (29.5)	32 (49.2)	17 (53.1)
Moderate	130 (47.6)	95 (54)	23 (35.4)	12 (37.5)
Severe	42 (15.4)	29 (16.5)	10 (15.4)	3 (9.4)
Unilateral or bilateral n(%)				
Both eyes	212 (77.4)	151 (84.4)	42 (67.2)	18 (58.1)
Don't know	7 (2.6)	2 (1.1)	3 (4.2)	2 (6.5)
Other eye disease n(%)				
Yes	112 (41.2)	78 (44.3)	25 (37.9)	9 (30)
Don't know	13 (4.8)	7 (4)	5 (7.6)	2 (6.7)
Glaucoma as main diagnosis n(%)				
Yes	134 (87.6)	94 (88.7)	31 (83.8)	10 (83.3)
Don't know	6 (3.9)	5 (4.7)	2 (2.8)	
One topical treatment n(%)				
Yes	246 (90.4)	161 (91.1)	58 (89.2)	29 (90.6)
Previous glaucoma surgery n(%)				
Yes	109 (39.9)	75 (41.9)	26 (39.4)	10 (31.3)
Previous laser surgery n(%)				
Yes	72 (26.5)	49 (27.5)	18 (27.3)	7 (21.9)
Don't know	4 (1.5)	2 (1.1)	3 (3.0)	
Annual income				
Less than £10,000	46 (19.1)	26 (15)	17 (34)	4 (19.1)
£10001–£20000	83 (34.5)	58 (33.6)	16 (32)	9 (42.8)
£20001–£30000	52 (21.5)	42 (24.3)	6 (12)	5 (23.8)
£30001+	60 (24.9)	47 (17.2)	11 (22)	3 (14.3)

[a]Total questionnaires returned (N) = 293, number of responses for each item varied. % are based on the available data.

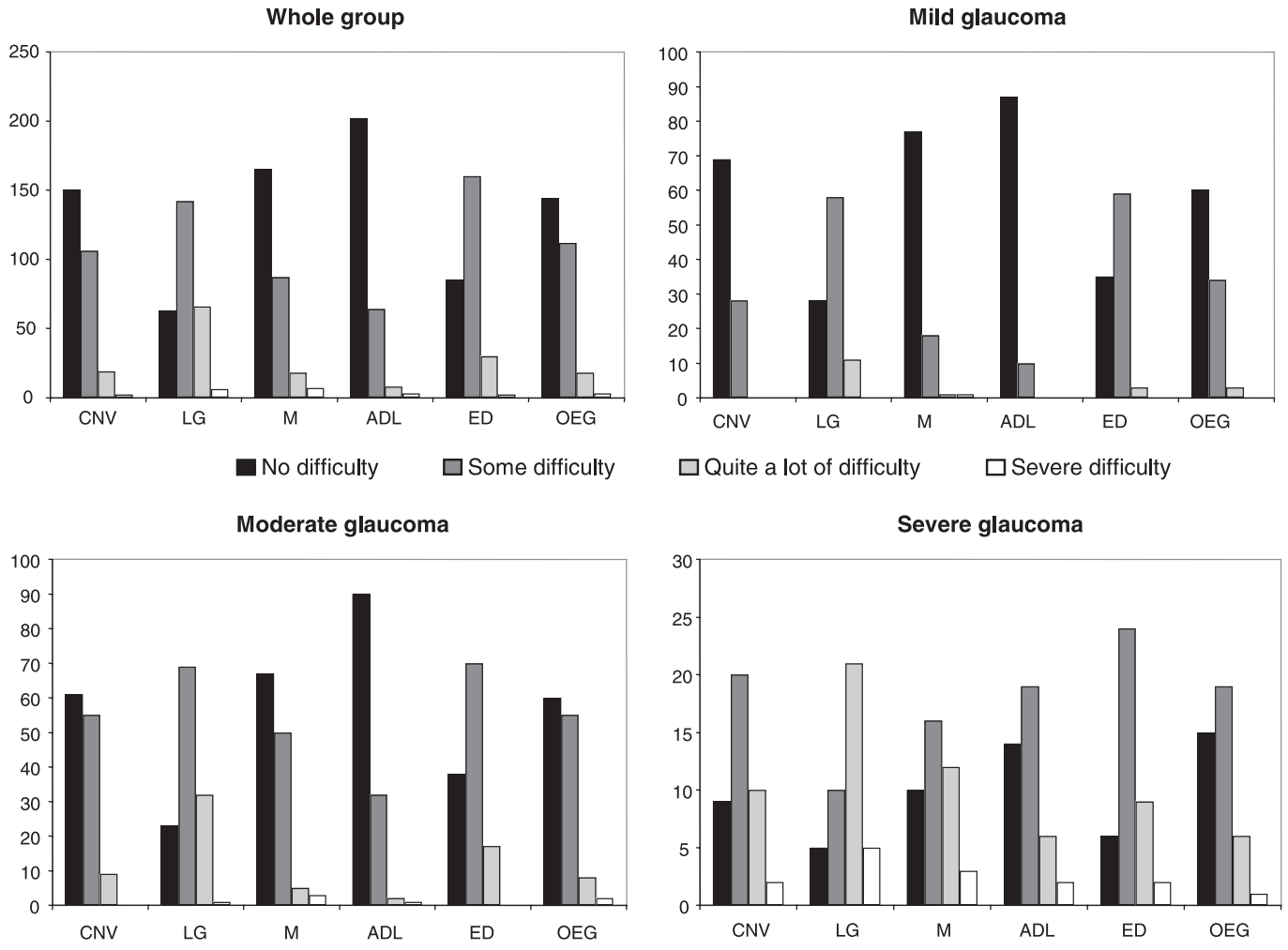

FIGURE 2.

Glaucoma Profile Instrument responses by dimension for the whole group and according to self-reported glaucoma severity. CNV refers to the dimension central and near vision, LG to lighting and glare, M to mobility, ADL to activities of daily living, ED to eye discomfort, and OEG to other effects of glaucoma.

disability and symptoms, supporting the validity of the developed GPI.

Two hundred and eighty-nine subjects responded to the DCE component of the questionnaire. Three respondents failed both consistency tests and were excluded from the regression analysis. Table 4 presents the final regression model, merging where levels within dimensions did not significantly differ. These results confirm the theoretical validity of the model, with coefficients increasing as the level of the dimension moves from severe to "better" levels. Moving from "no difficulty" with central and near vision to "severe difficulty" results in the most loss of utility followed by activities of daily living and mobility, systemic ("other effects"), and eye discomfort were considered to be the least important.

Quality weights, on a 0 to 1 scale, for each level of each dimension are detailed in Table 5. No difficulty with central and near vision gives a quality of weight of 0.322, moving to a situation where one has some difficulty will reduce the weight to 0.219 and moving to a situation where one has quite a lot of difficulty reduces the weight to 0.135. These quality weights can be summed to establish a quality weight or score for all profiles. Table 6 gives an example for four profiles.

Preferences were related to levels of self-reported severity ($\chi^2 = 331$; $p = 0.001$). Two dimensions were the main drivers: central and near vision and activities of daily living. For these dimensions significant differences ($p < 0.05$) were found between self reported mild and severe glaucoma as well as self-reported moderate and severe glaucoma. These differences were found for all three levels. More detailed results are available from the authors.

Table 7 reports the relationship between self-reported and clinically assessed responses to the severity of glaucoma question and the VAS, EQ-5D, and our generated GUI. Utility estimates derived from the GUI decreased as expected with increasing severity, defined both subjectively (self reported) and objectively (classified by increasing visual field loss). The results from EQ-5D and VAS reflect a similar trend. Utility estimated by the GUI was higher for mild glaucoma, compared with the VAS and the EQ-5D, but with increasingly severe glaucoma, by self report, the GUI appeared to be more sensitive with lower scores compared with the EQ-5D and the VAS. This was particularly apparent for severe glaucoma with a utility estimate of 0.64 ($\pm$0.22). The differences were variable and less apparent for severity graded by the severity of the binocular

TABLE 4.
Regression model

Dimension	Coefficient	p	95% Confidence interval
Central and near vision			
No difficulty	1.253653	0.000	1.162657–1.344649
Some difficulty	0.851563	0.000	0.753261–0.949865
Quite a lot of difficulty	0.526467	0.000	0.445376–0.607558
Lighting and glare			
No, some and quite a lot of difficulty	0.272127	0.000	0.200991–0.343262
Mobility			
No difficulty	0.920951	0.000	0.832372–1.00953
Some difficulty	0.577113	0.000	0.479041–0.675184
Quite a lot of difficulty	0.348718	0.000	0.261779–0.435657
Activities of daily living			
No difficulty	0.998826	0.000	0.910206–1.087447
Some difficulty	0.719518	0.000	0.621727–0.817309
Quite a lot of difficulty	0.430964	0.000	0.347294–0.514634
Eye discomfort			
No difficulty	0.240827	0.000	0.15831–0.323345
Some and quite a lot of difficulty	0.134489	0.000	0.056508–0.21247
Other effects			
No difficulty	0.201992	0.000	0.123405–0.280579
Some and quite a lot of difficulty	0.168744	0.000	0.08722–0.250268

Omitted reference categories severe difficulty for all dimensions.
Number of observations 16,606.
LR $\chi^2(14)$ 1818.02. Prob. χ^2 0.0000. Pseudo R^2 0.1579.

visual field loss. However, these estimates are based on small numbers of respondents in each severity category.

DISCUSSION

This article has advocated the use of the DCE methodology to estimate quality weights within the QALY framework. It was shown that the resulting regression equation could be used to estimate utility weights within the framework of a program-specific QALY measure. Following the development of the GPI, a GUI was estimated with utility weights for each level of each dimension. Central and near vision was the most important factor for people with glaucoma, systemic and local side effects of glaucoma treated were considered the least important. This agrees with two recent studies using similar methodology to assess the relative importance of aspects of visual loss and treatment effects related to glaucoma.[24,25]

A number of limitations of this study should be noted both in the development of the GPI, and in the use of DCE methodology to estimate utility weights. The content of the GPI was determined by qualitative research, although only two focus groups were convened and this may be considered as too small a sample. However, our methods were robust in that we used other validated profile instruments in particular the Glaucoma Quality of Life-15 (GQL-15) questionnaire developed by Nelson and colleagues,[5] and expert opinion in glaucoma (J.B.) to inform the framework of the focus group discussions and then modified the existing instruments according to the views of our patient group. The content area of the GPI is consistent with the GQL-15 relating to disability,[5] but includes additional dimensions related to side effects from treatment, highlighted from our focus group study as important factors. One of the difficulties in this study was incorporating all the important items of quality of life into the GPI and the relevant content area had to be grouped into broader dimensions. This was necessary for the DCE approach as the more dimensions and levels used in the DCE to determine the quality weights for the GPI the more difficult the choices become.[42]

The DCE questionnaire included two rationality tests. Such tests in DCEs have mainly involved investigating whether individuals choose dominated options (referred to in the literature as nonsatiation or dominance tests). However, it has been argued that such tests are easy to satisfy and that they may question the credibility of such experiments.[43] More stringent tests include transitivity (if choice A is preferred to B, and choice B is preferred to choice C, then choice A should be preferred to choice C) and Sen's expansion and contraction properties (see above). Here we included the latter tests, with only three respondents failing both tests. Although transitivity was not employed, one other study applying this test within a DCE found that only 6% of respondents failed, again providing support for the rationality of responses to DCEs.[47]

The response rate of 62% is good for an experiment of this nature.[43] Despite this, issues are raised concerning the representativeness of respondents. The approaches used to identify our study sample may not necessarily have reached all glaucoma sufferers, particular deprived populations, and all ethnic groups. However, the majority of respondents (85%) reported mild or moderate glaucoma and this is consistent with results from population surveys estimating glaucoma prevalence,[48,49] although these studies may also be prone to selection bias. The target sample included people with glaucoma identified from specialist clinics, and from a

TABLE 5.
Quality weights for the Glaucoma Utility Index

Dimension	Index[a]
Central and near vision	
No difficulty	0.322
Some difficulty	0.219
Quite a lot	0.135
Severe	0
Lighting and glare	
No difficulty	0.070
Some difficulty	0
Quite a lot	0
Severe	0
Mobility	
No difficulty	0.237
Some difficulty	0.148
Quite a lot	0.090
Severe	0
Activities of daily living	
No difficulty	0.257
Some difficulty	0.185
Quite a lot	0.111
Severe	0
Eye discomfort	
No difficulty	0.062
Some difficulty	0.035
Quite a lot	0.035
Severe	0
Other effects	
No difficulty	0.052
Some difficulty	0.043
Quite a lot	0.043
Severe	0

[a]When using DCEs to assess utility scores within a QALY framework, issues arise with anchoring on a 0 to 1 scale. To ensure the best level of all dimensions resulted in a score of "1" quality weights were calculated by summation of the coefficients associated with the best level for each dimension. The weights for all other levels of each dimension were then estimated as a proportion of this score, allowing all combinations to be estimated on a 0 to 1 scale while maintaining the ratio between the comparisons.

TABLE 6.
Utility scores for examples of alternative health state profiles

Situation description	Quality weights	Utility score
You have no difficulty with central and near vision You have no difficulty with lighting and glare You have no difficulty with mobility You have no difficulty with activities of daily living You have no difficulty with local eye discomfort You have no difficulty with other effects of glaucoma and its treatment	0.322 0.070 0.237 0.257 0.062 0.052	1
You have some difficulty with central and near vision You have no difficulty with lighting and glare You have no difficulty with mobility You have no difficulty with activities of daily living You have no difficulty with local eye discomfort You have no difficulty with other effects of glaucoma and its treatment	0.219 0.070 0.237 0.257 0.062 0.052	0.897
You have some difficulty with central and near vision You have some difficulty with lighting and glare You have some difficulty with mobility You have no difficulty with activities of daily living You have no local eye discomfort You have no difficulty with other effects of glaucoma and its treatment	0.219 0 0.148 0.257 0.062 0.052	0.737
You have severe difficulty with central and near vision You have severe difficulty with lighting and glare You have severe difficulty with mobility You have severe difficulty with activities of daily living You have severe difficulty with local eye discomfort and You have severe difficulty with other effects of glaucoma and its treatment	0 0 0 0 0 0	0

patient organization with glaucoma severity defined by self-report, apart from the Aberdeen subgroup where clinical validation of severity was also possible. Self-definition of health status will vary between participants, and from clinically validated severity. It is thus recognized that this sample was opportunistic, that health status was by self-report which is not standardized and therefore the utility weights may not be representative of the glaucoma population. People with severe glaucoma may not have been able to engage in the study, which was demanding in that the DCE questionnaire was lengthy, the whole questionnaire taking a median time of 75 min to complete. A large font size was used, but it still may have restricted the sample to people with the earlier stages of glaucoma. Thus it is possible that our findings do not reflect the preferences of people with more severe disease.

Following on from this, we found that preferences varied according to respondent's level of severity. This finding raises issues for policy makers. Although decisions on how to provide care might be most appropriately based on population preferences,[13] individual group preferences are then implicitly being ignored. This is an important general issue in the move to more patient centered care. However, this subgroup analysis relied on self rating

TABLE 7.
Utility scores, estimated by the Glaucoma Utility Index, EQ5D and the Visual Analogue Scale according to self-reported and objective assessment (binocular visual field loss) of glaucoma severity

	Glaucoma Utility Index (GUI)		EQ-5D		Visual Analogue Scale	
Severity	Self-report	Objective assessment	Self-report	Objective assessment	Self-report	Objective assessment
Mild glaucoma						
Valid	97	38	100	37	99	34
Missing[a]	4	2	1	3	2	6
Mean (SD)	0.87 (0.10)	0.84 (0.11)	0.83 (0.13)	0.80 (0.13)	0.82 (0.14)	0.76 (0.17)
Moderate glaucoma						
Valid	125	13	129	14	124	14
Missing[a]	5	3	1	2	6	2
Mean (SD)	0.79 (0.15)	0.77 (0.19)	0.81 (0.15)	0.75 (0.19)	0.81 (0.14)	0.79 (0.17)
Severe glaucoma						
Valid	41	9	42	9	40	9
Missing[a]	1	1	0	1	2	1
Mean (SD)	0.64 (0.22)	0.73 (0.17)	0.73 (0.20)	0.71 (0.25)	0.74 (0.17)	0.76 (0.14)

[a]Respondents provided details of glaucoma severity but did not complete the outcome measure.

of glaucoma severity, and further research is required to confirm these findings according to clinically classified glaucoma severity.

The analysis found no significant differences between coefficients for levels of three dimensions: lighting and glare; eye discomfort; and other effects. This suggests the index measure could be simplified by including only two levels of difficulty, "none" or "difficulty" for these dimensions. However, this finding may indicate that respondents had difficulty in making trade-offs between different levels of dimensions. Although respondents all had experience of glaucoma, thus potentially reducing the presence of nontrading behavior, this is clearly an important area for future research.

An important issue raised in the estimation of preference weights is that of scaling. The utility scale in our study was scaled between the "worst" profile (severe difficulty on all dimensions), and "best" profile (no difficulty on all dimensions). This approach is useful when developing a program-specific QALY. However, generic QALYS, typically estimated by SG and TTO, scale between perfect health and death, thereby allowing disparate health care interventions to be compared on a common scale. Within a DCE the problem of scaling may be overcome, by including, for example, death as a choice. However, this would be an unrealistic choice for people with glaucoma. An alternative is to rescale by using the TTO method alongside the DCE.[50] Adopting this approach would also allow investigation of where on the 0.0 (death) to 1.0 (perfect health) scale "perfect health with blindness" lies.

As noted above, previous studies of utility in the area of visual impairment have found no, or only a weak relationship between utility and visual impairment.[20] The above analysis, anchoring between death and perfect health, would allow investigation of this research question.

A further limitation recognized in the DCEs literature is that different dimensions may have a different underlying scale. This results in it being difficult to distinguish the importance of the overall weight of a given dimension from the importance of the levels within a weight. This has implications at the policy level because it is not possible to identify which—weight or scale—is influencing the statistical results. Within the context of this study, preferences can be influenced by (1) weight changes in any of the six dimensions; (2) dimension level changes for any of the six dimensions; or (3) both. If a level has high importance within a dimension, but the dimension carries little weight, then repositioning on that dimension is unlikely to influence preferences. One way to overcome this problem, currently being developed as a complement to the DCE approach, is that of Best-Worst Scaling.[51] Using this, in addition to the choices, respondents are asked to state the least attractive feature of each choice and the most attractive feature. This allows dimensions to be defined on the same underlying scale, in which one level of one dimension serves as the origin of the scale. Future work should explore the application of this technique for glaucoma specifically, and visual impairment more generally.

The strength of our study is that it is the largest study of its kind investigating patient reported effects related to glaucoma, and identifies dimensions of health of importance to people with glaucoma and estimates the relative importance of levels of these dimensions. This study has developed an instrument for estimating glaucoma-specific health status, the GUI, weighted using DCE methods. The algorithm developed could be used to readily score the responses to a short questionnaire (see Appendix) that might be administered as part of a randomized controlled trial or as a means of monitoring a patient's symptoms over time. The GUI has construct validity in that the utility scores derived from responses to the GUI are sensitive to glaucoma severity with the expected trend of decreased utility with increasing glaucoma severity. This trend was apparent for glaucoma assessed both by self-report and with increasing binocular visual field restriction. The glaucoma-specific measure appeared to be more sensitive with lower scores with increasing severity compared with the EQ-5D and the VAS. Comparisons with the EQ-5D and VAS are difficult, as they are elicited using very different tools and are scaled between death and full health but convergent validity is demonstrated.

The study also provides an estimate of the utility loss according to glaucoma severity. Such data would be useful in situations re-

searchers are attempting to use the techniques of systematic review and decision analytic modeling to estimate the relative effectiveness and cost-effectiveness of different treatments for glaucoma. In particular, the scores presented in this study or from future work can be used to populate an economic model with the necessary utility values required to estimate condition specific QALYs. When combined with cost information the cost-effectiveness of alternative interventions for glaucoma can be estimated.[11]

In summary, this article developed a preference-based outcome measure for evaluating glaucoma interventions. Following the development of the profile instrument, a DCE was used to estimate an index of quality weights for all outcomes within the instrument. The utility weights demonstrated theoretical, and convergent validity. Future work is required to assess the generalizability of the results to those with severe glaucoma. Such work may consider redefining levels where there was no significant difference between levels. On a methodological level, future research should focus on alternative methods of scaling. In addition, future studies should evaluate the reliability, validity, and responsiveness of the GUI in an adequately sized study representing people with all stages of glaucoma severity.

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APPENDIX

The appendix is available online at www.optvissci.com.

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Appendix: The Glaucoma Profile Instrument

Tick one box (✓), for each of the categories 1-6, which best describes any difficulties you have had in the last month with your eyes or vision, wearing your usual glasses.

You may need to refer back to the guide "Guide to aspects of quality life that may be affected in glaucoma and associated levels of difficulty" to help you answer these questions.

1. Central and near vision
For example difficulties with reading, watching TV and computer use?

None	☐
Some	☐
Quite a lot	☐
Severe	☐

2. Lighting and glare
For example difficulties with adjusting from light to dark and vice-versa, bright lights may dazzle, difficulties seeing in dim light?

None	☐
Some	☐
Quite a lot	☐
Severe	☐

3. Mobility
For example difficulties with crossing roads, driving, negotiating steps, kerbs, busy pavements etc?

None	☐
Some	☐
Quite a lot	☐
Severe	☐

4. Activities of daily living
For example difficulties with household or DIY tasks, pouring liquids into containers, putting crockery into cupboards, shaving etc?

None	☐
Some	☐
Quite a lot	☐
Severe	☐

5. Eye discomfort
For example difficulties with gritty, sore, tired eyes?

None	☐
Some	☐
Quite a lot	☐
Severe	☐

6. Other effects
For example fatigue, shortness of breath, dry mouth, bitter taste etc?

None	☐
Some	☐
Quite a lot	☐
Severe	☐