Associations among Visual Acuity and Vision- and Health-Related Quality of Life among Patients in the Multicenter Uveitis Steroid Treatment Trial

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Purpose. To evaluate the associations between visual acuity and self-reported visual function; visual acuity and health-related quality of life (QoL) metrics; a summary measure of self-reported visual function and health-related QoL; and individual domains of self-reported visual function and health-related QoL in patients with uveitis.

Methods. Best-corrected visual acuity, vision-related functioning as assessed by the NEI VFQ-25, and health-related QoL as assessed by the SF-36 and EuroQoL EQ-5D questionnaires were obtained at enrollment in a clinical trial of uveitis treatments. Multivariate regression and Spearman correlations were used to evaluate associations between visual acuity, vision-related function, and health-related QoL.

Results. Among the 255 patients, median visual acuity in the better-seeing eyes was 20/25, the vision-related function score indicated impairment (median, 60), and health-related QoL scores were within the normal population range. Better visual acuity was predictive of higher visual function scores ($P \leq 0.001$), a higher SF-36 physical component score, and a higher EQ-5D health utility score ($P < 0.001$). The vision-specific function score was predictive of all general health-related QoL ($P < 0.001$). The correlations between visual function score and general quality of life measures were moderate ($\rho = 0.29$–0.52).

Conclusions. The vision-related function score correlated positively with visual acuity and moderately positively with general QoL measures. Cost–utility analyses relying on changes in generic healthy utility measures will be more likely to detect changes when there are clinically meaningful changes in vision-related function, rather than when there are only changes in visual acuity. (ClinicalTrials.gov number, NCT00132691.) (*Invest Ophthalmol Vis Sci.* 2012;53:1169–1176) DOI:10.1167/iovs.11-8259

Metrics evaluating quality of life (QoL) have gained importance with the introduction of cost-effectiveness analysis (CEA). CEA attempts to evaluate whether an improvement in health due to a new form of treatment is worth the cost of the treatment.[1] In practice, these analyses require data on general health-related QoL, specifically measures of health utility, to be generalizable across different treatments and diseases. In patients with uveitis specifically and eye disease in general, there is a paucity of research on the relationship of general health-related QoL and health utility metrics with visual acuity, an often used and clinically important outcome for evaluating the effectiveness of treatments for ocular diseases, or vision-related functioning. Vision-related functioning is a broader measure than visual acuity, because it evaluates patients' ability to conduct activities of daily living (e.g., reading, driving, and face recognition) for which peripheral vision, and contrast and color vision, as well as visual acuity, are important.[2] Previously, visual acuity and vision-related functioning have been shown to be strongly related in patients with other eye diseases,[3] and

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QoL scores are lower in uveitis patients than in healthy controls, especially among patients with significant vision loss.[4] However, the degree to which standard health utility measures change with clinically meaningful differences in visual acuity or vision-related functioning is uncertain for patients with uveitis and limited visual acuity impairment.

Studying the relationships in the path from visual acuity to visual function to generic health-related QoL (particularly health utility) for patients with uveitis specifically is worthwhile because uveitis differs from other conditions affecting visual acuity. Uveitis is a collection of approximately 30 diseases characterized by intraocular inflammation that are collectively an important cause of visual loss in the developed world.[5,6] Because noninfectious uveitis often strikes at a younger age than many common eye disorders, such as cataract, macular degeneration, and glaucoma, it has a disproportionately high impact on years of potential vision lost and workplace or home-based productivity effects.[7] In addition, pain is sometimes associated with uveitis that is not associated with other conditions, and visual acuity often fluctuates rather than being stable.

The Multicenter Uveitis Steroid Treatment (MUST) Trial was designed to evaluate the comparative effectiveness of a systemic treatment strategy, primarily oral corticosteroids that may be supplemented with immunosuppressive drugs, to the fluocinolone intraocular implant.[8] The primary outcome of the MUST Trial is the change in best corrected visual acuity after 2 years of follow-up. The study also collected data on several QoL metrics, including self-reported vision-related functioning assessed with the National Eye Institute Visual Function Questionnaire (NEI VFQ-25), health-related QoL assessed with the Medical Outcomes Study 36-Item Short Form (SF-36), and health utility assessed with the EuroQoL EQ-5D questionnaire. We present the associations between measures of vision (visual acuity and vision-related function) and the more general measures of QoL and heath utility that were obtained at enrollment in the MUST trial. Our objective, for patients with uveitis, was to test relationships between (1) visual acuity and specific elements of visual function; (2) visual acuity and summary measures of visual function and generic health related QoL; (3) visual function and the QoL measures, to allow for possible mediation; and (4) specific elements of visual function and health-related QoL, to further explore relationships from the third test.

Methods

The MUST Trial

The methods for the MUST Trial have been presented elsewhere.[8] In brief, it was a randomized comparative effectiveness trial of the fluocinolone intraocular implant versus standardized systemic administration of corticosteroids supplemented with corticosteroid-sparing immunosuppressive drugs, as appropriate for the treatment of noninfectious intermediate, posterior, and panuveitis. Eligible patients had intermediate, posterior, or panuveitis, for which systemic treatment with oral corticosteroids was indicated in one or both eyes, there were no contraindications for treatment with either strategy, and vision was at least hand motion in the affected eye. Patients (n = 255) were enrolled at 23 clinical centers in the United States (21 centers), United Kingdom, and Australia from December 2005 through December 2008. Informed consent was obtained for all randomized patients. Institutional review boards approved the trial at each clinical and resource center. The trial was conducted in accordance with the Declaration of Helsinki and is a registered clinical trial.

Measures

At enrollment, each study participant's uveitis was classified by type as intermediate, posterior, or panuveitis. Measurements were made of visual acuity, self-reported vision-related function, and self-reported health-related QoL and health utility. Best-corrected visual acuity was measured in standard letters using the Early Treatment for Diabetic Retinopathy Study (ETDRS) logarithmic charts[9] and was reported in terms of the number of lines read (i.e., dividing the standard letters by 5). For example, a difference of one line corresponds to the difference in Snellen visual acuity between 20/20 and 20/25 or between 20/160 and 20/200. Participants were also classified into three functional vision categories based on best corrected acuity in the better-seeing eye. The categories were 20/40 or better (driving vision),[10] 20/41 to 20/199, and 20/200 or worse (legal blindness).[11]

Self-reported vision-related function was measured using the National Eye Institute Visual Function Questionnaire (NEI VFQ-25).[2,12] This 25-item questionnaire is used to generate a single composite score that ranges from 0 to 100, with 100 being the maximum visual function; a 4- to 6-point difference is considered clinically meaningful.[13] The overall composite score is the mean of the subscale scores for general vision; ocular pain; near activities; distance activities; driving; color vision; peripheral vision; and vision-specific social functioning (e.g., seeing facial expressions), mental health (e.g., frustration or embarrassment), role difficulties, and dependency on others to perform visual tasks.

Health utility was measured with the EuroQol questionnaire, which is composed of two metrics. The first is the EQ-5D, a five-question measure of health utility based on societal preferences, a method generally preferred for cost-effectiveness analyses.[14,15] Five questions ask about anxiety/depression, pain, mobility, usual activities, and self-care (essentially activities of daily living). For each question a respondent indicates that he or she does not experience the problem, experiences it moderately, or experiences it severely. The scores range from a maximum of 1 (not having any of the problems) to lower than 0, where an overall score of 0 is the health utility of death; a difference of 0.06 to 0.07 is considered clinically meaningful.[16,17] Utilities for the United States were developed in a study of several thousand respondents in which each person was asked to make tradeoffs among health states; hence, the utilities are based on societal preferences. The second measure was the EQ-Visual Analog Scale (VAS), a single item on which the individual indicates a personal valuation of current health on a vertical thermometer labeled from 0 to 100. It is a measure of personal health state valuation and not a measure of vision. For the EQ-VAS, 100 is the best health state imaginable, and 0 is the worst health state imaginable; a difference of 7 is considered clinically meaningful.[16] This personal valuation of health is shaped by what individuals think may be the worst imaginable health state and is not based on trade-offs.

The SF-36 was used to measure health-related QoL and produces a normative score that is not based on tradeoffs.[18] The SF-36 responses are coded as scores for eight domains (physical functioning, role physical, bodily pain, general health, vitality, social functioning, role emotional, and mental health) as well as separate physical and mental component summary scores (referred to as PCS and MCS, respectively). The score is scaled to a population norm, with a mean of 50 and an SD of 10; a difference of 3 to 5 points is considered clinically meaningful for the PCS scale.[19]

Analyses

Median and interquartile ranges were calculated for all the EuroQoL, SF-36, and VFQ-25 composite scores as well as for the SF-36 and VFQ-25 subscale scores. The Kruskal-Wallis test was used to compare the distributions of the scores between patients with intermediate uveitis and those with posterior or panuveitis.

Regression models were used to evaluate the relationship between (1) visual acuity and self-reported vision-related function, (2) visual acuity and health-related QoL, and (3) vision-related function and health-related QoL. The measurement of visual acuity used was the best corrected visual acuity in the better-seeing eye. Similar models were created for best corrected visual acuity in the worse-seeing eye,

but results are not shown here. Self-reported vision-related function was measured by the VFQ-25, and health-related QoL was measured by the EuroQoL and SF-36 questionnaires. Analyses were restricted to individuals able to read letters on visual acuity charts (i.e., eliminating hand motion only), which excluded a single individual from the better eye analysis. All multivariate regression models controlled for age, sex, race/ethnicity, and education. We explored controlling for the presence of a chronic, systematic, comorbid condition. As the adjustment did not alter the results substantially, we did not include the indicator in the final model.

Ordinary linear regression was used to construct the models described above when the outcome measure was normally distributed (i.e., for the outcome of the VFQ-25 composite and all VFQ-25 subscale scores except for the vision-specific social functioning scale). Robust linear regression using an M estimator with Tukey's biweight function[20] was used to construct the models for which the outcome measure was skewed (i.e., the VFQ-25 vision-specific social functioning scale, the SF-36 PCS and MCS, and the EuroQol EQ-VAS). For analyses in which the EQ-5D index score was the outcome measure, the scores were grouped into quartiles and proportional odds logistic regression was used to estimate associations. This approach was chosen because more than one in four participants had the maximum EQ-5D score of 1.0 (i.e., perfect health, with no limitations in any of the five domains) and the remainder of the distribution of EQ-5D scores was highly skewed toward the maximum.

To further explore the relationship between vision-related function and health-related QoL, Spearman correlation coefficients were used to estimate the strength of association between VFQ-25 (composite and the 12 domains) and the SF-36 component summary scores (PCS and MCS) or the EQ-5D or EQ-VAS scores.

Results

The characteristics of the 255 study participants have been published elsewhere.[8] Briefly, the population was predominantly white (56%) and female (75%), with an average age of 46 years (interquartile range, 34–56 years). Most (62%) had posterior or panuveitis and 89% had bilateral uveitis; 80% had no systemic disease associated with their uveitis diagnosis. At enrollment, the median time from the initial diagnosis of uveitis was 3.8 years (interquartile range, 1.2–8.0 years). The median visual acuities in the better- and worse-seeing eyes were 78 (20/25 Snellen equivalent) and 59 (20/63 Snellen equivalent) standard letters, respectively (Table 1). Only 79 (31%) of the participants had a best corrected visual acuity in the better-seeing eye worse than driving vision (Snellen equivalent $<$20/40 or $<$70 letters), and 12 (5%) had a best corrected visual acuity worse than legal blindness (Snellen equivalent of $\leq$20/200 or $\leq$35 letters).

The median overall composite score for self-reported vision-related functioning as measured by the VFQ-25 was 62; median subscale scores ranged between 45 for vision-specific mental health and 100 for color vision.

Median EQ-5D and EQ-VAS values for study participants were 0.8 and 80, respectively, with no significant differences between participants with intermediate versus those with pos-

Table 1. Visual Acuity and Questionnaire Scores of the Uveitis Participants at Baseline

	All Patients (n = 255)		Intermediate (n = 97)		Panuveitis (n = 158)		
Measure (Range, Direction)	**Median**	**IQR**	**Median**	**IQR**	**Median**	**IQR**	***P****
Best corrected visual acuity (−10 to 100, ↑)†							
Better eye, standard letters	78	66–86	80	64–87	77	66–85	0.47
Worse eye, standard letters	59	30–75	61	35–75	57	29–75	0.56
VFQ-25 subscales (0–100, ↑)							
General health	65	55–78	60	52–78	65	55–78	0.13
General vision	55	40–65	55	40–65	55	40–65	0.87
Ocular pain	75	50–88	75	50–88	75	50–88	0.67
Near activities	58	35–75	62	42–79	58	33–75	0.27
Distance activities	58	38–79	67	42–83	55	38–75	0.05
Vision-specific social functioning	75	58–92	83	67–100	75	50–92	0.07
Vision-specific mental health	45	25–65	45	20–65	45	25–65	0.73
Vision-specific role difficulties	56	38–75	56	38–75	56	38–75	0.51
Vision-specific dependency	69	38–94	75	44–94	69	38–94	0.55
Driving	50	0–75	58	0–75	42	0–75	0.12
Color vision	100	75–100	100	75–100	100	75–100	0.28
Peripheral vision	75	50–75	75	50–100	50	25–75	0.01
VFQ-25 (overall composite)	62	44–78	66	47–81	60	44–77	0.18
EuroQoL questionnaire (0–1, ↑)							
EQ-5D	0.8	0.8–1.0	0.8	0.8–1.0	0.8	0.8–1.0	0.44
EQ-VAS	80	67–90	75	60–87	80	70–90	0.22
SF-36 health survey subscales (0–100, ↑)							
Physical functioning	51	42–57	51	42–55	52	40–57	0.57
Role-physical	49	28–56	49	35–56	49	28–56	0.84
Bodily pain	54	44–63	54	44–63	54	45–63	0.66
General health	48	38–55	45	36–53	48	36–52	0.05
Vitality	49	40–58	49	40–58	49	40–59	0.89
Social functioning	52	35–57	52	41–57	49	35–57	0.18
Role-emotional	55	45–55	55	34–55	55	45–55	0.96
Mental health	50	41–57	50	44–57	50	39–57	0.56
Physical component summary	50	41–55	50	41–55	50	41–55	0.77
Mental component summary	52	40–57	52	43–57	52	37–56	0.56

* Difference between patients with intermediate uveitis and panuveitis, based on Wilcoxon rank sum test.

† Best corrected visual acuity measure in standard letters using logarithmic charts (85 = 20/20, 70 = 20/40, 55 = 20/80, and 35 = 20/200).[14]

TABLE 2. Associations between Visual Acuity in the Better-Seeing Eye and the NEI VFQ-25 Subscale Scores in Patients with Uveitis

Subscale	Association of Subscale Score with 1-Line Difference in Visual Acuity (n = 254)	P*
Linear regression, mean (95% CI)†		
General health	0.56 (−0.11 to 1.23)	0.99
General vision	2.89 (2.31 to 3.48)	<0.001
Ocular pain	1.42 (0.60 to 2.24)	0.001
Near activities	3.99 (3.21 to 4.76)	<0.001
Distance activities	4.62 (3.00 to 4.59)	<0.001
Vision-specific social functioning	3.95 (3.09 to 4.74)	<0.001
Vision-specific mental health	2.89 (2.01 to 3.77)	<0.001
Vision-specific role difficulties	4.02 (3.17 to 4.87)	<0.001
Vision-specific dependency	4.68 (3.75 to 5.62)	<0.001
Peripheral vision	3.49 (2.53 to 4.45)	<0.001
Logistic regression, OR (95% CI)‡		
Driving	1.62 (1.40 to 1.91)	<0.001
Color vision	1.24 (1.13 to 1.36)	<0.001

* Regression models adjusted for age, sex, race/ethnicity, and education; subscale scores range from 0 to 100, with higher scores indicating better function.

† Mean change in subscale score associated with 1-line difference in visual acuity estimated from linear regression model with adjustment.

‡ Odds ratio (OR) associated with odds of being in higher functioning category (i.e., score higher than median value) from logistic regression model adjusted for age, sex, race/ethnicity, and education.

terior or panuveitis. The SF-36 summary scores and subscale scores medians were close to population norms of 50, ranging from a low median of 48 for general health to the high median of 55 for emotional role function.

A 1-line better visual acuity score (5 standard letters higher) in the better-seeing eye was predictive of higher subscale scores ($P \leq 0.001$; Table 2) with the exception of the general health subscale score ($P = 0.99$; Table 2) and of a higher score in the overall VFQ-25 composite score (3.65 points on average; Table 3). Better visual acuity in the better-seeing eye also predicted higher scores on two of the four general measures of QoL: EQ-5D and SF-36 PCS but not EQ-VAS or SF-36 MCS (Table 3). When participants were classified into three functional categories based on visual acuity in the better eye (20/40 or better, 20/41–20/199, or 20/200 or worse), there were strong positive associations ($P < 0.0001$) with the median VFQ-25, SF36-PCS, and EQ-5D scores. The median SF36-PCS was 51, 47, and 34 for those functional visual acuity categories, respectively, and median EQ-5D scores were 80, 75, and 70, respectively. These functional categories were not associated with SF-36 MCS ($P = 0.75$) or EQ-VAS scores ($P = 0.11$). In analyses in which worse-eye acuity was the independent predictor, results were similar but associations were weaker (data not shown).

The ability of the NEI VFQ-25 composite score, the measure of vision-related function, to predict general health-related QoL and health utility measures was also evaluated. On average, patients who reported higher scores on the VFQ-25 composite score had higher scores for the EQ-VAS, SF-36 PCS, and SF-36 MCS ($P < 0.001$; Table 4). For the EQ-5D, a higher composite score on the VFQ-25 was associated with increased odds of a better health state (i.e., being in a higher quartile of EQ-5D).

Correlations between the VFQ-25 composite and subscale scores and visual acuity and the EQ-5D, EQ-VAS, and SF-36 component scores are summarized in Table 5. The correlations between the VFQ-25 subscales and the EQ5D and SF-36 scales were in general in the range of what is considered a moderate correlation ($\rho = 0.3–0.5$) with a few strong correlations ($\rho \geq 0.5$).[21] The strongest correlation was between the VFQ-25 general health and the EQ-VAS ($\rho = 0.70$, 95% confidence interval [CI] 0.64–0.76). All the VFQ-25 subscales correlated at least moderately with the EQ-5D score (correlations ranging from $\rho = 0.31–0.52$). Most of the VFQ-25 subscales (all but general vision, driving, and color vision) also correlated mod-

TABLE 3. Associations between Visual Acuity in the Better-Seeing Eye and Scores of Overall VFQ-25, SF-36, and EuroQoL Questionnaires in Patients with Uveitis

Questionnaire Score	Association of Score Value with 1-Line Difference in Visual Acuity (n = 254)	P*
Linear regression, mean (95% CI)†		
VFQ-25	3.65 (3.04 to 4.27)	<0.001
SF-36 PCS	0.55 (0.07 to 1.03)	0.004
SF-36 MCS	0.01 (−0.49 to 0.53)	0.96
EQ-VAS	0.37 (−0.40 to 1.11)	0.27
Logistic regression, OR (95% CI)‡		
EQ-5D	1.13 (1.05 to 1.21)	<0.001

* Regression models adjusted for age, sex, race/ethnicity, and education; subscale scores range from 0 to 100, with higher scores indicating better function.

† Mean change in subscale score associated with 1-line difference in visual acuity estimated from linear regression model with adjustment.

‡ OR associated with EQ-5D outcome (categorized into four ordered levels at the quartiles from lowest to highest quartile) from proportional odds logistic regression.

TABLE 4. Associations between the NEI VFQ-25 Composite Score and SF-36 and EuroQol Questionnaires in Patients with Uveitis

Questionnaire Score	Association of Score Value with a 10-Point Difference in VFQ-25 Score (n = 254)	P*
Linear regression, mean (95% CI)†		
SF-36 PCS	1.95 (1.39 to 2.51)	<0.001
SF-36 MCS	2.12 (1.29 to 3.01)	<0.001
EQ-VAS	2.38 (1.25 to 3.56)	<0.001
Logistic regression, OR (95% CI)‡		
EQ-5D	1.82 (1.49 to 2.01)	<0.001

* Regression models adjusted for age, sex, race/ethnicity, and education; subscale scores range from 0 to 100, with higher scores indicating better function.

† Change in subscale score associated with 1-line difference in visual acuity estimated from linear regression model with adjustment.

‡ OR associated with EQ-5D outcome (categorized into four ordered levels at the quartiles from lowest to highest quartile) from proportional odds logistic regression.

erately with the SF-36 PCS. In contrast, only the general health, vision-specific mental health, and vision-specific dependency VFQ-25 subscales correlated moderately with the EQ-VAS score and the SF-36 MCS, which is consistent with the overall lower correlation between the VFQ-25 composite score and EQ-VAS and SF-36 MCS.

DISCUSSION

Our results are for a population with, on average, minimal impairment in visual acuity in the better eye (median best corrected visual acuity of 20/25 Snellen equivalent). However, our patients reported more significant impairment in vision-related function (mean visual function score = 60), similar to patients with macular edema or with choroidal neovascularization[13] and well below a mean score of over 90 in patients without eye disease.[2,22] The general QoL measures were within U.S. population norms for SF-36 scores. The EQ-5D median score of 0.80 fell between scores of individuals who ranked their health as good (0.84) or fair (0.71).[23] The median EQ-VAS was 80, close to population norms for men and women age 30 to 60 years (VAS 85 to 90, respectively).[24]

Visual acuity in the better eye was predictive of vision-related function scores. For the well-established clinical difference of two lines on an ETDRS chart (e.g., 20/20 Snellen to 20/32 Snellen), visual acuity was predictive of a greater than 6-point (2 × 3.56) higher vision-related function score, which is considered to be clinically meaningful. There were more modest positive associations between visual acuity in the better eye and two measures of overall health (SF36 PCS and EQ-5D). These associations were more evident when patients were grouped into functional categories on the basis of visual acuity in the better eye, indicating that these generic measures are sensitive to functional differences in visual acuity.

Our finding of a statistically significant relationship between visual acuity in patients with uveitis and self-reported vision-related function replicates findings reported previously in populations with uveitis and other eye diseases. In India, researchers used an instrument reflecting visual function (similar to the NEI-VFQ but consisting of 33 items in Tamil) and found that it was related to visual acuity and responsive to treatment.[25] Gardiner et al.[26] found that binocular visual acuity was associated with vision-related function but that the visual acuity in neither the better nor the worse eye was associated with vision-related function, when analyzed in a step-wise regression approach. Our patients showed similar associations between visual acuity in the better eye and NEI-VFQ score (ρ = 0.66) and similar mean overall vision-related function score as those of patients with macular degeneration, choroidal neovascularization, diabetic retinopathy, and age-related macular degeneration,[13,27] and their mean score was markedly reduced

TABLE 5. Spearman Correlation Coefficients between QoL Scales for Patients with Uveitis

	EuroQoL Questionnaire		SF-36 Health Survey	
	EQ-5D	EQ-VAS	PCS	MCS
VFQ-25 subscale				
General health	0.51 (0.41 to 0.59)	0.70 (0.64 to 0.76)	0.56 (0.47 to 0.64)	0.41 (0.30 to 0.51)
General vision	0.32 (0.20 to 0.43)	0.23 (0.11 to 0.34)	0.24 (0.12 to 0.35)	0.14 (0.02 to 0.26)
Ocular pain	0.46 (0.35 to 0.55)	0.28 (0.17 to 0.39)	0.41 (0.30 to 0.51)	0.28 (0.16 to 0.39)
Near activities	0.45 (0.35 to 0.54)	0.23 (0.11 to 0.34)	0.34 (0.23 to 0.45)	0.19 (0.07 to 0.31)
Distance activities	0.46 (0.36 to 0.55)	0.20 (0.08 to 0.31)	0.35 (0.24 to 0.45)	0.20 (0.07 to 0.31)
Vision specific social functioning	0.42 (0.32 to 0.52)	0.21 (0.09 to 0.32)	0.35 (0.24 to 0.45)	0.28 (0.16 to 0.39)
Vision specific mental health	0.50 (0.40 to 0.59)	0.32 (0.20 to 0.43)	0.34 (0.23 to 0.45)	0.47 (0.37 to 0.56)
Vision specific role difficulties	0.48 (0.38 to 0.57)	0.27 (0.16 to 0.38)	0.45 (0.35 to 0.54)	0.28 (0.16 to 0.39)
Vision specific dependency	0.50 (0.40 to 0.58)	0.32 (0.21 to 0.43)	0.38 (0.27 to 0.48)	0.39 (0.29 to 0.49)
Driving	0.32 (0.20 to 0.43)	0.12 (−0.01 to 0.25)	0.27 (0.15 to 0.39)	0.13 (0.00 to 0.26)
Color vision	0.31 (0.20 to 0.42)	0.08 (−0.05 to 0.20)	0.27 (0.15 to 0.38)	0.14 (0.02 to 0.26)
Peripheral vision	0.36 (0.25 to 0.46)	0.19 (0.07 to 0.31)	0.32 (0.21 to 0.43)	0.20 (0.08 to 0.31)
VFQ-25 (overall composite)	0.52 (0.43 to 0.60)	0.29 (0.17 to 0.40)	0.43 (0.32 to 0.53)	0.31 (0.19 to 0.42)
Visual acuity, better eye	0.24 (0.12 to 0.35)	0.10 (−0.02 to 0.22)	0.20 (0.08 to 0.32)	0.00 (−0.12 to 0.12)

Data are shown as the Spearman rank correlation coefficient (95% CI).

from the mean NEI-VFQ score of patients without ocular disease.[16]

Murphy et al.[28,29] found that change in visual acuity in the worse-seeing eye correlated only moderately with a change in vision-related functioning and that there was no association between change in vision-related functioning and of change in visual acuity in the better-seeing eye. Our current evaluation is cross-sectional, and so we could not evaluate dynamic associations. However, we did find that associations were typically stronger for visual acuity in the better-seeing eye. It is possible that change in vision-related function with change in visual acuity, which may be more dramatic in the worse-seeing eye, is associated more strongly with the worse-seeing eye, whereas the cross-sectional associations of vision-related function are more related to visual acuity in the better eye. However, if the overall state of an individual is more strongly associated with vision in the better-seeing eye because the better-seeing eye is a stronger determinant of functionality, our focus on analysis of visual acuity in the better eyes is warranted.

Miserocchi et al.[4] found that visual acuity was related to the SF-36-measured QoL of patients with chronic noninfectious uveitis on systemic immunosuppressive treatment. Our results showed a weaker association of visual acuity with SF36 PCS than theirs did and we found a statistically significant but weak relationship between visual acuity and the EQ-5D score. Polack et al.[30] and van Nispen et al.[31] have also demonstrated a direct association between poor visual acuity and worse EQ-5D scores in older populations with visual impairment due to cataract or other ocular disease. Our results are also consistent with a study that addressed a slightly different question, estimation of the relationship between the EQ-5D and self-reported blindness compared with self-reported normal vision[32] This study showed that the difference in score between blindness and normal vision was 0.07—also suggesting a small-magnitude but consistent statistically significant relationship between visual acuity and health utility.

Associations between self-reported vision-related function score and general health-related QoL including health utility measures were stronger than associations of visual acuity with these more general measures. Self-reported vision-related function captures different aspects of vision-related health and well-being and may be able to integrate multiple components, such as peripheral vision and color vision, that contribute to good vision, but are not captured by visual acuity measurements. Schiffman et al.[33] found a relationship between the NEI-VFQ and the PCS and MCS of the SF-36 in patients with uveitis. Furthermore, we established a similar strong association of vision-related function with the EQ-5D scores and thereby extend the prior finding to include health utility measures, which are common in cost-effectiveness studies.

One way to extend the findings in this study in the future would be to consider subgroups of patients, particularly those who may be the target of clinical guideline recommendations. For example, patients with a high degree of ocular pain, or patients with panuveitis as opposed intermediate uveitis or patients with unilateral as opposed to bilateral uveitis may be the focus of specific recommendations. We performed analyses comparing groups by their response to a question about any ocular pain on the VFQ-25 and found little difference in the relationship between visual acuity and generic health related QoL. In the future, this issue could be examined in greater detail with additional questions focusing on specific aspects of ocular pain. For example, chronic pain may influence the relationship between visual acuity and QoL more than acute pain. Performing analyses of the relationship between visual acuity, visual function, and generic health-related QoL and understanding how this would affect the interpretation of cost-effectiveness results (for which each of the outcomes listed may be used as outcomes depending on the resource allocation question being addressed) is important.

The major limitations of our evaluation are that it was a cross-sectional analysis and may not reflect temporal associations among the measures and that most of our patients had no notable visual acuity impairment. Nevertheless, our cross-sectional findings suggest that vision-related function is a stronger predictor of meaningful differences in a general health-related QoL measure than is visual acuity. However, our population had relatively good visual acuity, and so findings may not generalize to patients who present initially with low visual acuity. Furthermore, patients with persistently low vision may make accommodations for poor visual acuity that weaken the association with general health-related QoL. Finally, the study's external validity is intended to generalize only to the uveitis patients who were eligible for the consideration of the implant as a part of their treatment.

These results suggest that cost-utility analyses relying on changes in generic healthy utility measures will be more likely to detect changes when there are clinically meaningful changes in vision-related function rather than when there are only changes in visual acuity. In this regard, self-reported vision-related function may be a promising proxy for utility of cost-effectiveness studies for treatments of uveitis and other eye diseases, and, at a minimum, should always be considered as a measure of treatment effect.

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APPENDIX

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Johns Hopkins University, *Baltimore*, *MD*: James P. Dunn (Director), Ellen Arnold, Jeff Boring, Diane M. Brown, Alison G. Livingston, Kisten Nolan, and Terry Reed. Former members: Marie-Lynn Belair, Stephen G. Bolton, Joseph B. Brodine, Lisa M. Brune, Anat Galor, Adam Jacobowitz, Meera Kapoor, Sanjay Kedhar, Henry A. Leder, Yavette Morton, George B. Peters, Priscilla Soto Ricardo Stevenson, Michelle Tarver-Carr, Yue Wang, and Stephen Kim.

Massachusetts Eye Research and Surgery Institute, *Cambridge*, *MA*: C. Stephen Foster (Director), Angelica Contero, Linda Bruner, Kayleigh Fitzpatrick, David M. Hinkle, Jyothir Johnson, Danielle Marvell, and Jennifer Pinto. Former members: Sarah Acevedo, Fahd Anzaar, Tom Cesca, Karina Q. Lebron, Chandra Morgan Nita Patel, Janet Sprague, and Taygan Yilmaz.

National Eye Institute, *Bethesda*, *MD*: H. Nida Sen, (Director), Denise Cunningham, Darryl Hayes, Dessie Koutsandreas, Nupura Krishnadev, Theresa Larson, Annal D. Meleth, Richard Mercer, Robert B. Nussenblatt, Patti R. Sherry, Gregory L. Short, Wendy Smith, and Alana Temple. Former members: Allison Bamji, Hanna Coleman, Geetaniali Davuluri, Lisa Faia, Chloe Gottlieb, Guy V. Jirawuthiworavong, Julie C. Lew, Dominic Obiyor, Cheryl H. Perry, Natalia Potapova, Eric Weichel, Keith J. Wroblewski, and Steven Yeh.

New York Eye and Ear Infirmary, *New York*, *NY*: Paul A. Latkany (Director), Jason Badamo, Jenny Gallardo, Monica Lorenzo-Latkany, Robert Masini, Susan Morell, Ann Nour, Meredith Sanchez, and Kate Steinberg. Former members: Kenneth M. Boyd, Jacek Jarczynski, and Mirjana McGrosky.

Royal Victorian Eye & Ear Hospital, *East Melbourne*, *Australia*: Richard J. Stawell (Director), Lisa Breayley, Julie Ewing, Carly D'Sylva, Lauren Hodgson, Ignatios Koukouras, Lyndell Lim, Cecilia Ling, Rachel McIntosh, Andrew Newton, Richard Smallwood, and Ehud Zamir. Former members: Nicola Hunt, Lisa Jones, and Suzanne Williams.

Rush University Medical Center, *Chicago*, *IL*: Pauline T. Merrill (Director), Pam Hulvey, Elaine Kernbauer, Scott Toennessen, and Denise L. Voskuil-Marre. Former members: Bruce Gaines, Christina Giannoulis, Heena S. Khan, and Sarah J. Levine.

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