

Activity Limitation in Glaucoma: Objective Assessment by the Cambridge Glaucoma Visual Function Test

Simon E. Skalicky,¹⁻⁵ Colm McAlinden,⁶⁻⁸ Tasneem Khatib,² Louise May Anthony,² Sing Yue Sim,² Keith R. Martin,^{2,3} Ivan Goldberg,^{1,9,10} and Peter McCluskey^{1,10}

¹Discipline of Ophthalmology, University of Sydney, Sydney, Australia

²Addenbrookes Hospital, Ophthalmology Department, Cambridge, United Kingdom

³Cambridge NIHR Biomedical Research Centre, University of Cambridge, Cambridge, United Kingdom

⁴Departments of Ophthalmology and Surgery, Royal Melbourne Hospital, University of Melbourne, Melbourne, Australia

⁵Centre for Eye Research Australia, Royal Victorian Eye and Ear Hospital, University of Melbourne, Melbourne, Australia

⁶Abertawe Bro Morgannwg University Health Board, Swansea, United Kingdom

⁷School of Ophthalmology and Optometry, Wenzhou Medical University, Wenzhou, Zhejiang, China

⁸Flinders University, Bedford Park, Adelaide, South Australia, Australia

⁹Eye Associates, Sydney, Australia

¹⁰Glaucoma Unit, Sydney Eye Hospital, Sydney, Australia

Correspondence: Simon E. Skalicky, Royal Victorian Eye & Ear Hospital, 32 Gisborne Street, East Melbourne, Victoria 3002, Australia; seskalicky@gmail.com.

Submitted: February 29, 2016

Accepted: May 1, 2016

Citation: Skalicky SE, McAlinden C, Khatib T, et al. Activity limitation in glaucoma: objective assessment by the Cambridge Glaucoma Visual Function Test. *Invest Ophthalmol Vis Sci*. 2016;57:6158-6166. DOI:10.1167/iov.16-19458

PURPOSE. We design and evaluate a computer-based objective simulation of activity limitation related to glaucoma.

METHODS. A cross-sectional study was performed involving 70 glaucoma patients and 14 controls. Mean age was 69.0 ± 10.2 years; 49 (58.3%) were male. The Cambridge Glaucoma Visual Function Test (CGVFT) was administered to all participants. Rasch analysis and criterion, convergent, and divergent validity tests assessed the psychometric properties of the CGVFT. Regression modeling was used to determine factors predictive of CGVFT person measures. Sociodemographic information, better and worse eye visual field parameters, visual acuity, contrast sensitivity, and the Rasch-analyzed Glaucoma Activity Limitation-9 (GAL-9) and Visual Function Questionnaire Utility Index (VFQUI) questionnaire responses were recorded.

RESULTS. From 139 pilot CGVFT items, 59 had acceptable fit to the Rasch model, with acceptable precision (person separation index, 2.13) and targeting. Cambridge Glaucoma Visual Function Test person measure (logit) scores increased between controls (-0.20 ± 0.08) and patients with mild (-0.15 ± 0.08), moderate (-0.13 ± 0.10), and severe (-0.05 ± 0.10) glaucoma ($P < 0.001$, ANOVA) indicating good criterion validity. Correlation coefficients of 0.455 ($P < 0.001$) between CGVFT and GAL-9 person measures and 0.399 ($P = 0.005$) between CGVFT and VFQUI person measures demonstrated convergent validity. Divergent validity was suboptimal. On multivariable analysis, lower better eye mean deviation and greater age were associated with worsening CGVFT person measures ($P \leq 0.001$).

CONCLUSIONS. The CGVFT is a computerized visual challenge test administered to a cohort of glaucoma patients. It may benefit glaucoma patients, careers, health care providers, and policy makers, providing increased awareness of activity limitation due to glaucoma.

Keywords: Cambridge Visual Function Test, Rasch analysis, glaucoma, activity limitation

Patients with glaucoma of worsening severity have increasing difficulty performing visually demanding tasks requiring contrast discrimination, light/dark adaptation, and peripheral vision-dependent activities.¹ As glaucomatous optic neuropathy progresses it can impact driving, walking, venturing from home, reading, seeing at night, adjusting to different levels of illumination, judging distances, seeing peripheral objects, and moving objects coming from the side.^{2,3} Motor vehicle accidents and injuries related to falls are potentially serious consequences of glaucomatous visual loss.⁴

Patients with glaucoma experience reductions in contrast sensitivity (CS) early and then throughout the disease course,⁵ visual acuity (VA) loss late in the disease course, and gradual reduction in visual field sensitivity (measured primarily by mean deviation [MD]) from early to advanced disease; each can

influence daily visual function and quality of life (QoL).⁶ However, these clinical visual tests may not reflect real-world visual function. For example, external brightness differs from that within the clinic, and can vary throughout the day; unlike in visual field testing patients are able to move their heads and eyes and shift gaze during daily visual tasks.

Assessment of glaucoma-related activity limitation by questionnaire subjectively evaluates patients' ability to perform visually-related tasks; this has been shown to correlate with clinical markers of glaucoma severity.³ However, using questionnaires, also known as patient-reported outcomes (PROs) to evaluate vision-related functional impairment has limitations. Psychologic factors, personality, and recall bias may influence patients' responses.⁷



Many of these limitations could potentially be overcome by objective simulation of functional visual ability. A performance-based assessment of functional ability related to vision, the Assessment of Visual Disability Related to Vision (ADREV) has been engineered, validated and shown to correlate mainly with markers of central visual function (VA and CS).^{8,9}

We hypothesized that objective visual functional testing could be improved using simpler, more reproducible computer-simulated activities—as such, patients still can be tested in real-life simulations while seated safely, under timed conditions. Such testing may help bridge the gap in understanding between patients and clinicians as to how glaucoma may interfere with patients' daily life; it could be an important educational intervention for patients. Although a simple and easily useable form of such testing has not been designed previously, computer-based simulations may have a greater role in future activity limitation assessment and clinical management of glaucoma patients.

We aimed to design a computerized objective simulation test of visual ability in patients with glaucoma that is repeatable, simple to perform and reflective of everyday tasks.

METHODS

Subjects

Participants were recruited from subspecialty glaucoma clinics in Cambridge, United Kingdom, in 2013 at a large university-associated teaching hospital. During regular follow-up visits, eligible subjects were approached consecutively and invited to participate in the study after providing informed consent. The study adhered to the tenets of the Declaration of Helsinki. Ethical approval was provided by the local hospital network Human Research and Ethics Committee.

Eligibility for this study included the ability to speak, read, and comprehend English fluently and age over 40 years. To be eligible for the glaucoma group, participants required a diagnosis of chronic open-angle glaucoma (OAG) in one or both eyes. Open-angle glaucoma was diagnosed based on an open anterior chamber angle on gonioscopy, characteristic glaucomatous optic disc changes (including rim loss, notching, and/or significant nerve-fiber layer bundle loss), and/or glaucomatous visual field loss demonstrated on the Humphrey Visual Field Analyzer (HFA; Humphrey Instruments, Inc., Zeiss Humphrey, San Leandro, CA, USA). Glaucomatous visual field loss was defined based on previously defined Anderson criteria.¹⁰ Controls were patients attending the clinics with ocular hypertension or glaucoma suspects; they did not have visual field test results that met Anderson's criteria nor had glaucomatous optic disc changes on either side.

Patients with any nonglaucomatous condition that might influence visual function, such as visually-significant cataract (Lens Opacities Classification System III greater than Grade 2), nonglaucomatous optic neuropathy or other neuro-ophthalmic condition, retinal or macular pathology, or ocular laser or surgery in the previous 3 months were excluded from the study, as were patients without reliable visual field test indices (based on previously defined criteria).¹¹

Assessment of Clinical Parameters

Achromatic perimetry was performed using the HFA Swedish Interactive Threshold Algorithm standard 24-2 test. For all measured visual parameters the better eye (BE) was determined based on the visual field index (VFI); when equivalent between eyes, the MD was used. Snellen VA was recorded and converted to the logarithm of the minimum angle of resolution

(logMAR). Contrast sensitivity was recorded using the Pelli-Robson chart monocularly.

Clinical markers of visual function from the BE and worse eye (WE) may each influence vision-related QoL.^{12,13} For this reason clinical markers of visual function (CS, VA, MD, pattern standard deviation [PSD]) and VFI) from the BE and WE were used in regression modeling. Significant scotomata (based on Anderson criteria) on visual field testing were assessed for either a central (involving at least one of the central four loci on the 24-2 test printout) or peripheral (not involving any of the central four loci) location. Some monocular visual field printouts had scotomata located centrally and peripherally.

The Nelson glaucoma staging system (GSS) was used to stratify glaucoma severity.¹⁴ This involved three groups of patients: "mild" (unilateral deficit of less than half of the visual field), "moderate" (unilateral deficit of more than half of the visual field, or deficit of less than half of the visual field in each eye), or "severe" (loss of more than half of the visual field in each eye). This GSS strongly correlates with perimetric MD and PSD calculated from binocularly integrated data.¹⁴

Subjective Assessment of Vision-Related Activity Limitation

Glaucoma-related activity limitation was assessed subjectively by the Rasch analysis of Glaucoma Activity Limitation 9 (GAL-9) questionnaire, which was derived from Rasch analysis of the Glaucoma Quality of Life (GQL)-15 questionnaire.³ The GAL-9 comprises 9 items that correlate with severity of visual field loss.¹⁵ Each item-level response was coded on a scale of one to five: one signifies no difficulty and five signifies severe difficulty.^{3,15}

The Visual Function Questionnaire Utility Index (VFQUI) was used to assess global vision-specific QoL. The VFQUI is a six-item, second generation PRO derived from reengineering and Rasch analysis of the National Eye Institute Visual Function Questionnaire (NEIVFQ-25) with improved psychometric properties.¹⁶

Assessment of Other Risk Factors

Sociodemographic details were obtained by self-report. Covariates included age (years), sex, education level, employment status, marital status, and ethnicity.

GAL-9 and VFQUI

Rasch analysis was used to assess the psychometric properties of the GAL-9 and VFQUI using the Andrich rating scale model with Winsteps software (version 3.81; Chicago, IL, USA).¹⁷ During Rasch analysis, ordinal questionnaire summary scores are estimated on an interval scale (expressed in logits). For the GAL-9 and VFQUI, increasing person measure (in logits) indicates greater activity limitation.¹⁵

The Cambridge Glaucoma Visual Function Test (CGVFT)

The CGVFT was designed by two of the study investigators (SES and TK) taking inspiration from ADREV items as well as daily challenges described by patients with glaucoma (See Supplemental Material S1. The Cambridge Glaucoma Visual Function Test).³ A total of 13 tasks of visual function related to glaucoma and reflective of daily life were included. Each task had three to four difficulty levels (easy, moderate, challenging and very difficult) that were attempted by each participant. The tasks simulated: (1) identifying objects in a busy street scene, (2) identifying individuals in a group or crowd, (3)

identifying unique daily objects surrounded by similar objects, (4) identifying creatures in camouflaged environments, (5) identifying cutlery in a cluttered cutlery drawer, (6) identifying objects within a cluttered room, (7) identifying hazardous furniture in a dimly illuminated room, (8) identifying an article in a sheet of newspaper, (9) identifying an “x” within a set of “+’s”, (10) identifying a match for a sock, (11) identifying moving balls coming to the center from the periphery in multiple directions, (12) reading with progressively reduced contrast, and (13) performing a road hazard-perception driving-simulation test.

The CGVFT was administered to participants by one of the test administrators (TK, SYS, LMA, or SES). All administrators conferred before commencement of testing and following testing to ensure strict and consistent adherence testing protocols as maintained by the principal investigator (SES). The background lighting conditions of the room were kept completely dark with 5 minutes of dark adaptation time provided for the participants. The computer image was projected onto a 3 × 1 m white screen at a distance of 1 m reflecting a 60° horizontal visual field. A portable liquid-crystal display projector was linked to a MacBook Air (Macintosh; Apple, Cupertino, CA, USA) to project the image at a distance of 4 m from the screen, at a brightness of 3000 American National Standards Institute lumens and resolution 1024 × 768 pixels. The images were a series of slides designed on Powerpoint (Microsoft Corporation 2010; Redmond, WA, USA). Each image represented a specific task that the participant was asked to complete by the test administrator.

Each image has a central fixation point of a rotating gold star, and participants were asked to begin each task by looking specifically at the fixation point but were subsequently permitted eye and/or head movements to complete the task. Participants were monitored by the test invigilator to ensure their gaze was initially on the central gold rotating star. The eye movement options permitted to the participant during the test may reflect how glaucoma patients use saccades to complete daily tasks.¹⁸

Most items within the test were timed. For each timed item, timing was commenced from the moment the administrator finished reading the task instructions until the participant verbally indicated correct identification of the object or completed the task. Results were recorded for untimed tasks in a pass/fail manner (See Supplemental Material S2. The Cambridge Visual Function Test Scoresheet).

Rasch Analysis of the CGVFT

Rasch analysis was used to assess the psychometric properties of the CGVFT. Details regarding the methods of Rasch analysis can be found from previous studies.^{15,17,19}

The commercial software Winsteps (version 3.70.0.2; Winsteps) was used in this study to run the Rasch analyses. The pilot CGVFT contained 139 items in total. These included items with “Yes/No” categories, an item with six categories (0, 1, 2, 3, 4, 5), and items with two parts. The first part was a “Yes/No” category and the second part was timed in seconds which was only applicable if the patient answered “Yes” to part one. Principal component analysis of the residuals was performed to identify clusters of items (contrasts with an eigenvalue >2 units and item loading ≥0.4).²⁰ Clusters of items were assessed for item fit to the Rasch model. Infit and outfit statistics may be reported as a mean-square (MNSQ) with an ideal fit of 1.²¹ An acceptable range for clinical observations is 0.50 to 1.70 which was set as the criterion in this study.²² The person separation index is used to illustrate how many strata of person ability an instrument can discriminate.¹⁵ The minimum acceptable person separation for this study was set at 2.²³

Targeting reflects the matching of patient ability to item difficulty and can be graphically visualized with a person-item map. Traditionally, targeting can be assessed by comparing the mean patient and item values, ideally with a mean difference of zero. Significant mistargeting can be classified with differences greater than one.²⁴

Category collapsing typically is used in questionnaire development or validation.^{25,26} As the CGVFT is not a questionnaire but a test of competency at a specific task with a timed result, categories were not considered for collapse as each time in seconds is entirely possible.

Statistical Analysis

Statistical Package for Social Sciences (SPSS, Inc., Chicago, IL, USA) for Mac (version 21.0; Microsoft Corporation) was used for statistical analyses.

The sample size calculation was based on the modeled standard error of the item calibration. The modeled standard errors are in the range: $2/[\sqrt{\text{sample size}}] < \text{standard error} < 3/[\sqrt{\text{sample size}}]$. A sample size was calculated to achieve 95% confidence that any item calibration is within 0.5 logits from its modeled standard error, which equates to a required sample size in the range of 64 to 144.²⁷ Hence, the minimum acceptable sample size set for this study was 64.

To account for subject dropout we aimed to recruit slightly greater numbers, with the ratio of controls to glaucoma patients 1:4 to 5 in keeping with previous studies evaluating visual function in glaucoma.^{7,28,29}

Demographic variables, BE VA and CS, BE visual field parameters (VFI, MD, and PSD), CGVFT, and GAL-9 (logit) scores were compared among controls, mild glaucoma, moderate glaucoma, and severe glaucoma patient groups. Intergroup significance was assessed using ANOVA for parametric data and the nonparametric Kruskal-Wallis analysis of ranks.

Validity Evaluation of the Cambridge Glaucoma Visual Function Test

The following tests were used to validate the CGVFT: criterion, convergent, and divergent validity.

Criterion Validity. Criterion validity of the CGVFT descriptive system was assessed by evaluating the ability of the CGVFT person scores to distinguish between the following groups: controls, mild, moderate, and severe glaucoma. Intergroup significance was assessed using ANOVA with 2-tailed *P* value considered significant at <0.05.

Convergent Validity. Convergent validity of the CGVFT descriptive system was assessed by exploring the correlation with the GAL-9 and the VFQUI using the Pearson correlation coefficient. We hypothesized there would be moderate correlation ($r = 0.4\text{--}0.7$) between the scores as they are measuring related constructs.

Divergent Validity. Divergent validity for the CGVFT was assessed by evaluating correlation between CGVFT person measures and factors (sex and sociodemographic data: marital status, employment status, and education level) that we would hypothesize to have no correlation with CGVFT person measures.

Regression Analysis

A univariable regression analysis was performed to examine the association between CGVFT person measure scores (logit) and the following variables: GAL-9 and VFQUI (logit) scores, age, sex, demographic data, and the following BE and WE data: MD, PSD, VFI, VA, CS, the presence of a peripheral scotoma, and the

TABLE 1. Participant Demographics and Clinical Characteristics ($n = 84$)

Variable	Controls, $n = 14$	Patients With Glaucoma			P Value
		Mild, $n = 24$	Moderate, $n = 32$	Severe, $n = 14$	
Mean age, y (SD)	62.8 (12.1)	68.0 (9.4)	71.7 (9.5)	70.5 (9.4)	0.049
Sex, n (%)					
Female	6 (42.9)	13 (54.2)	12 (37.5)	4 (28.6)	0.441
Male	8 (57.1)	11 (45.8)	20 (62.5)	10 (71.4)	0.441
Demographic data, n (%)					
Married/stable relationship	9 (64.3)	13 (54.2)	19 (59.4)	9 (64.3)	0.913
Tertiary education	8 (57.1)	8 (34.8)	12 (37.5)	6 (42.9)	0.573
Retired/unemployed	7 (50.0)	18 (75.0)	24 (75.0)	10 (71.4)	0.35
Caucasian	14 (100.0)	24 (100.0)	30 (93.8)	13 (92.9)	0.471
BE logMAR VA mean (SD)	-0.04 (0.12)	-0.004 (0.16)	0.09 (0.22)	0.17 (0.25)	0.013
BE MD mean dB (SD)	-0.17 (1.15)	-1.52 (2.40)	-3.76 (3.36)	-14.00 (8.01)	<0.001
BE PSD mean dB (SD)	1.84 (0.29)	2.25 (1.93)	3.95 (3.06)	9.33 (3.92)	<0.001
BE VFI mean % dB (SD)	98.7 (0.73)	96.7 (3.56)	92.6 (7.45)	59.6 (28.2)	<0.001
BE contrast sensitivity, log, mean (SD)	1.29 (0.19)	1.23 (0.23)	1.08 (0.26)	0.87 (0.44)	<0.001
WE logMAR VA mean (SD)	-0.043 (0.13)	0.042 (0.19)	0.36 (0.66)	0.86 (1.25)	0.001
WE MD mean dB (SD)	-1.09 (1.10)	-5.07 (3.83)	-12.49 (5.90)	-20.44 (7.68)	<0.001
WE PSD mean dB (SD)	2.03 (0.67)	6.17 (4.09)	9.58 (3.43)	10.45 (3.88)	<0.001
WE VFI mean % dB (SD)	97.4 (1.60)	85.6 (12.4)	66.1 (18.1)	38.8 (25.7)	<0.001
WE contrast sensitivity, log, mean (SD)	1.30 (0.17)	1.20 (0.23)	0.91 (0.35)	0.68 (0.51)	<0.001
GAL-9 score, logit, mean (SD)	-4.30 (1.43)	-3.13 (1.86)	-2.32 (1.39)	-0.50 (2.06)	0.003
VFQUI score, logit, mean (SD)	-6.21 (0.61)	-5.71 (2.19)	-4.89 (1.91)	-2.79 (3.57)	0.000

dB, decibels; NS, no significance; SD, standard deviation.

presence of a central scotoma. To evaluate for multicollinearity the correlation between all variables was assessed using Spearman's and Kendal tau b correlation tests for nonparametric data and Pearson's for parametric data. Variables with strong (>0.8) correlations were excluded from the regression modeling. All of these variables then were included in a stepwise linear multivariable analysis. All variables were assessed for normality and linearity and transformed as required, and analysis of residuals was performed. Independence of residuals was assessed using the Durbin-Watson statistic. All tests were 2-tailed with $P < 0.05$ considered significant.

RESULTS

The cohort consisted of 70 glaucoma patients (24 mild, 32 moderate, and 14 severe glaucoma) and 14 controls. Mean age was 69.0 (SD, 10.2) years and 49 (58.3 %) were male; 56 patients were excluded from this study due to the presence of lenticular opacity.

Table 1 outlines parameters compared among the following groups: controls, and mild, moderate, and severe glaucoma. The relative distribution of sex and demographic data did not differ significantly among groups. Better and WE visual field parameters (MD, PSD, and VFI), CS, and VA worsened with increasing glaucoma severity among groups. Rasch analysis of the Glaucoma Activity Limitation-9 and VFQUI logit scores increased (i.e., activity limitation worsened) with increasing glaucoma severity among groups.

GAL-9 and VFQUI

The GAL-9 scores displayed good fit to the Rasch model, with no evidence of multidimensionality, ordered thresholds, no differential item functioning or item misfit. Initially targeting and scale precision were suboptimal (difference between person and item means -2.61 and person separation index

[PSI] 1.7). Persons with "extreme" responses (i.e., those who responded "no difficulty" to all items, $n = 18$) were removed from Rasch analysis of the GAL-9, and targeting improved (-1.91) as did precision (PSI, 2.30) to acceptable levels.

Similarly, the VFQUI displayed good fit to the Rasch model, with no multidimensionality, ordered thresholds, differential item functioning, or item misfit. Targeting was poor (difference between person and item means -5.06) and PSI suboptimal (1.25). Upon removal of persons with "extreme" responses ($n = 35$) targeting improved marginally (-3.68) as did precision (1.77), but not to levels ideal for analysis.

Cambridge Visual Function Test Rasch Analysis

With the initial 139 items included, a PCA of the residuals was performed and the unexplained variance explained by the first contrast was 25.5 eigenvalue units, with 61 items loading (>0.4) onto the first contrast. The unexplained variance explained by the second contrast was 8.6 eigenvalue units, with 7 items loading (>0.4) onto the second contrast. The unexplained variance explained by the third contrast was 7.9 eigenvalue units, with 13 items loading (>0.4) onto the third contrast. The unexplained variance explained by the fourth contrast was 5.7 eigenvalue units, with six items loading (>0.4) onto the fourth contrast. The unexplained variance explained by the fifth contrast was 5.7 eigenvalue units, with six items loading (>0.4) onto the fifth contrast.

The items within each of the five contrasts formed five separate domains for further psychometric testing. For the first domain containing 61 items, a Rasch analysis was performed and the item fit statistics indicated that one item misfitted (item #92 [Task 5, item b]) due to an outfit MNSQ of 1.97. This item was removed and a second Rasch analysis performed. Item #103 (Task 8, Item d) was found to misfit with an outfit MNSQ of 1.72. This item was removed and a third Rasch analysis performed and the remaining 59 items were within the acceptable infit and outfit range. The person separation

TABLE 2. Steps Involved in Reducing the CGVFT From 139 to 59 Items

Step 1	Principal component analysis (PCA) of all 139 items
Step 2	Unexplained variance explained by the first contrast was 25.5 eigenvalue units, with 61 items loading (>0.4) onto the first contrast
Step 3	Two items were found to misfit (outside the range 0.50–1.70) and were removed: Item #92 and #103
Step 4	Assessment of person separation: 2.15 (acceptable)
Step 5	Assessment of targeting: difference of 0.13 between the mean patient and item values (acceptable)
Step 6	Rasch analysis of each of the second to fifth possible domains (from PCA) indicated that none provided valid measurement. Items were grossly misfitting and the person separation was inadequate.

statistic was acceptable with a value of 2.15. Targeting also was acceptable with a difference of 0.13 between the mean patient and item values. Rasch analysis of each of the second to fifth domains indicated that none provided valid measurement. Items were grossly misfitting and the person separation was inadequate (Table 2).

A CGVFT person measure (logit) score was created for each of the 84 subjects based on the 59 items that fit the Rasch model. The pilot items removed from the Rasch analyzed CGVFT have been marked with a strikethrough on Supplemental Material S2. The Cambridge Glaucoma Visual Function Test Scoresheet. An item person map outlining the relationship between person ability to item difficulty is provided in Supplemental Material S3. A Rasch-scaled scoring algorithm for the CGVFT is available on request which provides a linear transformation of ordinal CGVFT data.

CGVFT Validation in a Glaucoma Cohort

Criterion Validity. The CGVFT person measure scores (logit) distinguished between controls and patients with mild, moderate, and severe glaucoma with mean CGVFT person measures of -0.20 (SD 0.08), -0.15 (SD 0.08), -0.13 (SD 0.10), and -0.05 (SD 0.10), respectively ($P < 0.001$).

Convergent Validity. The Pearson correlation coefficient for CGVFT person measures with GAL-9 person measures was 0.455 ($P < 0.001$), and was 0.399 ($P = 0.005$) for CGFT with VFQUI person measures, indicating a moderate correlation between the Rasch-analyzed measures of vision-related functional limitation (Figs. 1, 2).

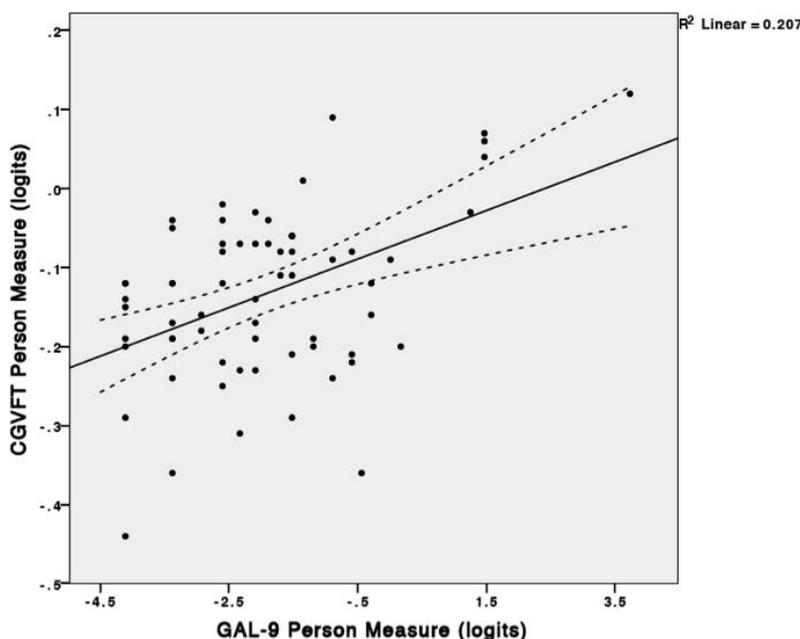
Divergent Validity. Weak correlation was detected between poorer CGVFT person measure (logit) scores and male sex (correlation coefficient, 0.243; $P = 0.008$) and being retired/unemployed (correlation coefficient, 0.221; $P = 0.015$). No significant correlation was detected for marital status (correlation coefficient, 0.195) or education level (correlation coefficient, 0.009).

Factors Predictive of CGVFT (Logit) Score: Univariable and Multivariable Analysis

Univariable and multivariable regression modeling were used to identify factors predictive of the CGVFT (logit) score.

Ethnicity was excluded from analysis as it was not a useful variable with such a large proportion (96.4%) being Caucasian. Univariable analysis revealed that worse GAL-9 scores; VFQUI scores; older age; male sex; being retired or unemployed; poorer BE and WE VA, MD, and CS; BE PSD; and the presence of a peripheral scotoma in the WE were associated with lower CGVFT person measure scores (Table 3). Education status, marital status, WE PSD, the presence of a central scotoma in either eye, and a peripheral scotoma in the BE were not significantly associated with CGVFT person measure scores. On multivariable regression modeling, lower BE MD (regression coefficient [β], 1.70; 95% confidence interval [CI], 1.32–2.18; $P < 0.001$) and greater age (β , 1.41; 95% CI, 1.13–1.76; $P = 0.001$) were independently associated with lower CGVFT person measures (Table 3). The variance (R^2) explained by the multivariable model was 0.477.

Figures 3 and 4 outline the scatter plot of CGVFT and GAL-9 person measures versus BE MD; each variable has similar relationship with BE MD (correlation coefficient, -0.441 [CGVFT] and -0.472 [GAL-9]). In comparison the VFQUI did

**FIGURE 1.** Scatterplot: CGVFT person measures versus GAL-9 person measures.

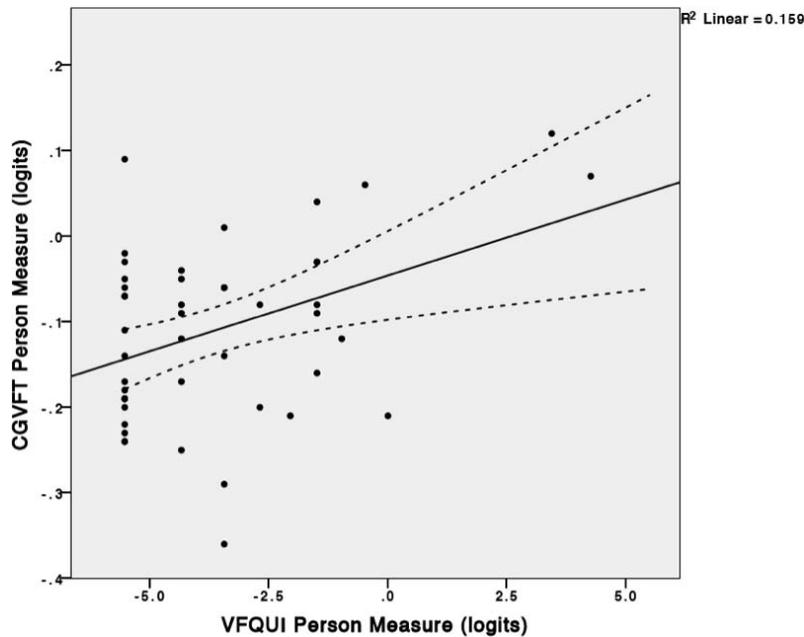


FIGURE 2. Scatterplot: CGVFT person measures versus VFQUI person measures.

not correlate significantly with BE MD (correlation coefficient, -2.79 ; $P = 0.052$).

DISCUSSION

We have designed a new computerized objective test that may simulate daily visual function related to glaucoma. This test was

evaluated for fit to the Rasch model and, following removal of misfitting items, had an overall good fit with good targeting and precision. The CGVFT was assessed successfully using criterion and convergent validity tests.

As this was the prototype test designed specifically to evaluate visual dysfunction related to glaucoma, patients with coexistent ocular comorbidities, like cataract, were strictly

TABLE 3. The Association Between Demographic, Clinical and Patient-Reported Outcome Variables and Cambridge Visual Function Test (Logit) Score in Univariable and Multivariable Regression Models ($P < 0.05$ Was Considered Significant)

Variable	β Coefficient	95% CI	R Statistic	F Statistic	P Value
Univariable analysis					
GAL-9 person measure	1.62	1.28–2.05	0.455	16.71	<0.001
VFQUI person measure	1.49	1.14–1.95	0.399	8.88	0.005
Age, older	1.58	1.30–1.92	0.459	21.86	<0.001
Male sex	1.28	1.03–1.58	0.244	5.18	0.026
Retired/unemployed	1.33	1.08–1.64	0.286	7.29	0.008
Tertiary education	1.01	0.81–1.26	0.009	0.007	0.933
Married/stable relationship	0.82	0.66–1.02	0.195	3.23	0.076
BE MD	1.59	1.31–1.93	0.466	22.76	<0.001
WE MD	1.4	1.15–1.70	0.36	11.62	0.001
BE PSD	1.43	1.16–1.75	0.356	11.91	0.001
WE PSD	1.17	0.95–1.43	0.164	2.16	0.146
BE central scotoma	1.09	0.86–1.37	0.081	0.511	0.48
WE central scotoma	1.2	0.96–1.51	0.185	2.65	0.11
BE peripheral scotoma	1.25	1.00–1.57	0.219	0.389	0.052
WE peripheral scotoma	1.56	1.26–1.92	0.439	17.87	<0.001
BE VA	1.54	1.25–1.86	0.422	17.76	<0.001
WE VA	1.55	1.27–1.89	0.438	19.48	<0.001
BE CS	1.63	1.34–1.98	0.492	25.28	<0.001
WE CS	1.67	1.37–2.02	0.51	28.08	<0.001
Multivariable analysis*					
BE MD	1.70	1.32–2.18	0.691	16.41	<0.001
Age	1.41	1.13–1.76			0.004

Bold items were significant to $P < 0.05$. Nonbold items were not significant factors on modeling. R and F statistics based on normalized data. * All significant variables on univariable analysis were modeled in stepwise linear multivariable analysis. Rasch analysis GAL-9-9 person measure, VFQUI person measure, sex, employment status, education status, marital status, WE MD, BE and WE PSD, BE and WE peripherally or centrally located scotomata, BE and WE VA, and BE and WE CS were not significant factors in the final multivariate model.

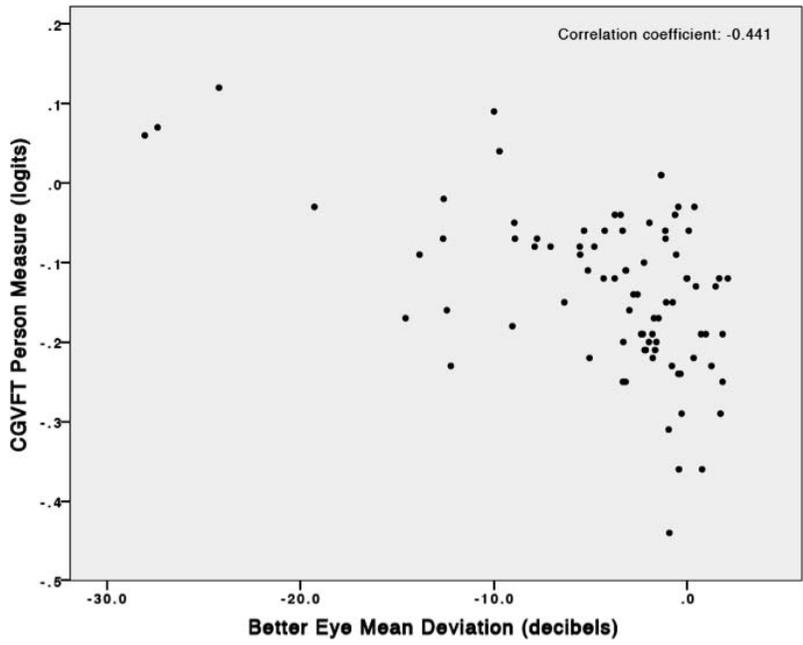


FIGURE 3. Scatterplot: CGVFT person measures versus BE MD.

excluded from this study. We acknowledge the important role of ocular and other comorbidities in influencing visual performance and QoL for glaucoma patients, and believe further studies evaluating the influence of these on CGVFT performance would be worthwhile.²⁹

The CGVFT was compared to the GAL-9 in terms of ability to reflect glaucoma severity and sample activity limitation related to glaucoma. With good Rasch metrics in glaucoma cohorts, the GAL-9 is a good measure activity limitation related to glaucoma.^{15,29} Compared to the GAL-9, the CGVFT has similar correlation with BE MD, PSI, and better targeting. The strength of the GAL-9 results in part from serial refinement over time.^{3,15} This is the first version of the CGVFT, which may

be improved with future modifications. In comparison the VFQUI, a global vision-related QoL measure, had poorer correlation with MD, PSI, and targeting among a glaucoma cohort than the glaucoma-specific GAL-9 and the CGVFT.

In our cohort divergent validity was suboptimal, and male sex and being unemployed/retired were associated with CGVFT person scores. This may be explained by a nonsignificant trend of increasing prevalence of male sex and unemployment with increasing glaucoma severity (Table 1). These factors were not significant on multivariable analysis for predictors of CGVFT, indicating they are proxy markers for other factors, like increasing age and BE MD.

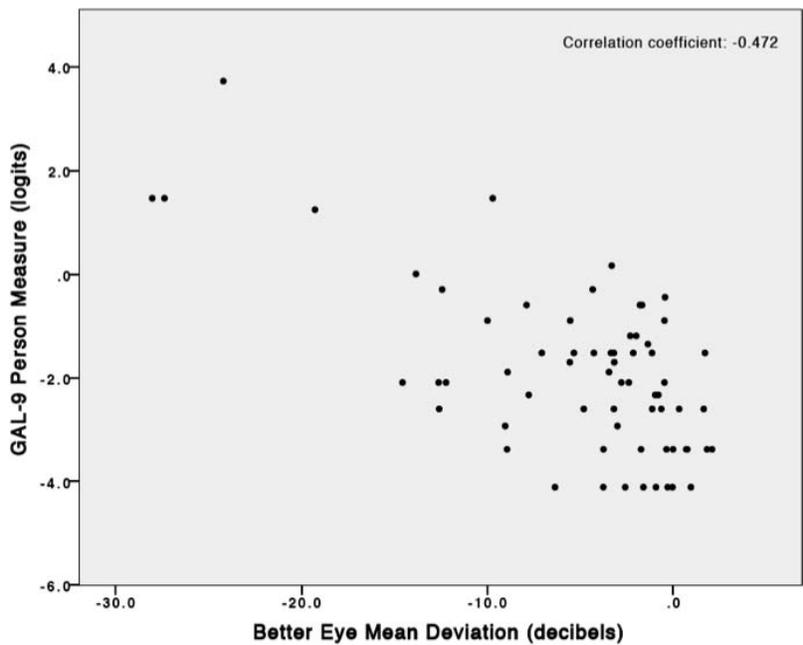


FIGURE 4. Scatterplot: GAL-9 person measures versus BE MD.

On multivariable analysis, worsening BE MD and increasing age were independent predictors of poorer patient ability on the CGVFT. Mean deviation is a marker of peripheral and central reduction in visual sensitivity related to glaucoma; this is probably why it is an important influence of CGVFT ability in this cohort. Age was another independent predictor of poor visual function on the CGVFT. Increasing age is associated with reduced VA,³⁰ CS,³¹ reaction time, and cognition;³² all of which may explain its relationship to the CGVFT person measure.

Visually significant scotomata were evaluated for a central or peripheral location. Although the presence of a peripheral scotoma in the WE was associated with poorer CGVFT ability, this was not significant on multivariable analysis. As each item in the CGVFT assesses a different location of the peripheral field, mapping the location of a visual field defect to overall CGVFT ability is challenging.

The CGVFT can be compared to the ADREV, the other objective visual function test described in the literature.^{8,9} The ADREV recently has been compressed into a 9-item version, the Compressed Assessment of Ability Related to Vision (CAARV).³³ Both ADREV and CAARV are physical tests, requiring much room space and maneuverability—this compromises accessibility and repeatability, poses difficulties in the clinical environment, and may cause physical mishaps during the test. Furthermore, outcomes may be influenced by neurologic or musculoskeletal morbidities and/or cognition.⁷ Recently, Warriani et al. suggested improving scoring of the ADREV by incorporating time taken to complete the tasks.³⁴ The ADREV initially was validated against the NEIVFQ-25, which is a generic multidimensional PRO with poor specificity to glaucoma and poor fitting to the Rasch model.¹⁶

Strengths of the CGVFT are as follows. The CGVFT is purely computer-based, allowing the test to be more widely, practically, and safely administered in the clinical environment, and minimizing other nonvisual clinical influences, such as neurologic and musculoskeletal disease. The test is timed, allowing fine gradations of visual function to be detected. It has moderate correlation with person measures of a Rasch-analyzed, glaucoma-specific activity limitation PRO, the GAL-9. As a simulation of real life scenarios, it may increase awareness for patients, their families, clinicians and policy makers about the potential impact of glaucoma on daily visual function. Patient-reported outcomes data suggest that while patients with early glaucoma may not be consciously aware of activity limitation, they have greater measured functional impairment compared to controls.³⁵ The CGVFT may detect early functional impairment; demonstrating a problem before the patient realizes there is one may help in early glaucoma detection and intervention.

This study has potential limitations. Our sample population was relatively uniformly Caucasian and derived from a subspecialty service from a tertiary referral teaching hospital; as such, it may not reflect the broader population of patients with glaucoma. While this study controlled for a range of potentially confounding covariates, additional variables, such as measures of cognitive performance, were not included; these may have influenced the results. A larger sample size would have been ideal; however, recruitment was challenging in the busy clinical environment, and the sample size for patients and controls was within the desired range. The VFQUI had suboptimal targeting and precision in a glaucoma cohort, rendering its reliability as a PRO in this study questionable.

In addition, the CGVFT has potential limitations. The test requires specific hardware (e.g., a computer, projector) as well as specific lighting and patient adaptation criteria. One cannot be certain if the CGVFT really reflects real-life tasks experienced by the patient; as such, tasks are impossible to precisely recreate and measure scientifically. Like all clinical tests and

PROs, the CGVFT is at best a potential sample of visual difficulties that might be experienced by glaucoma patients.

Patients were invigilated to begin each task by gazing on the rotating central golden star, but then allowed to break fixation to complete the task. This is not the same as true fixation control typically used for computerized visual field testing. However breaking fixation was necessary to complete most of the visual tasks—hence, a degree of eye and head movement was permitted. Future studies may be required to determine if the use of initial gaze centration enhances or detracts from the validity of this test.

Patients with glaucoma may actually achieve some compensatory responses in terms of eye or head movements to cope with limitations imposed by scotomas; these may greatly impact a patient's ability to succeed in visual challenges.¹⁸ In the CGVFT, the length of time before making the first eye movement (generally a saccade) and its speed and accuracy were not recorded; these may have influenced participants' ability on the CGVFT. This may be an important evaluation to include in future versions of the test potentially using gaze-tracking technology.

Potential avenues of improvement include the use of virtual reality software on smartphone technology that can be used to measure patients' ability to navigate a simulated three-dimensional environment from a remote observer computer screen.

CONCLUSIONS

The CGVFT is a computer-based test administered to a cohort of glaucoma patients and cohorts. This tool may benefit glaucoma patients, careers, health care providers, and policy makers, providing increased awareness of activity limitation due to glaucoma.

Acknowledgments

The authors thank Phuc Nguyen for his statistical advice.

Disclosure: **S.E. Skalicky**, None; **C. McAlinden**, None; **T. Khatib**, None; **L.M. Anthony**, None; **S.Y. Sim**, None; **K.R. Martin**, None; **I. Goldberg**, None; **P. McCluskey**, None

References

- Lorenzana L, Lankaranian D, Dugar J, et al. A new method of assessing ability to perform activities of daily living: design, methods and baseline data. *Ophthalmol Epidemiol*. 2009;16:107–114.
- Ramulu P, Maul E, Hochberg C, et al. Real-world assessment of physical activity in glaucoma using an accelerometer. *Ophthalmology*. 2012;119:1159–1166.
- Goldberg I, Clement CI, Chiang TH, et al. Assessing quality of life in patients with glaucoma using the Glaucoma Quality of Life-15 (GQL-15) questionnaire. *J Glaucoma*. 2009;18:6–12.
- Haymes SA, Leblanc RP, Nicoletta MT, Chiasson LA, Chauhan BC. Risk of falls and motor vehicle collisions in glaucoma. *Invest Ophthalmol Vis Sci*. 2007;48:1149–1155.
- Lahav K, Levkovitch-Verbin H, Belkin M, Glovinsky Y, Polat U. Reduced mesopic and photopic foveal contrast sensitivity in glaucoma. *Arch Ophthalmol*. 2011;129:16–22.
- Chan EW, Chiang PP, Liao J, et al. Glaucoma and associated visual acuity and field loss significantly affect glaucoma-specific psychosocial functioning. *Ophthalmology*. 2015;122:494–501.
- Skalicky S, Goldberg I. Depression and quality of life in patients with glaucoma: a cross-sectional analysis using the Geriatric Depression Scale-15, assessment of function related

- to vision and the Glaucoma Quality of Life-15. *J Glaucoma*. 2008;17:546-551.
8. Altangerel U, Spaeth GL, Steinmann WC. Assessment of function related to vision (AFREV). *Ophthalmol Epidemiol*. 2006;13:67-80.
 9. Richman J, Lorenzana LL, Lankaranian D, et al. Importance of visual acuity and contrast sensitivity in patients with glaucoma. *Arch Ophthalmol*. 2010;128:1576-1582.
 10. Anderson DR. *Automated static perimetry*. St Louis: Mosby 1992:123-133.
 11. Keltner JL, Johnson CA, Cello KE, et al. Visual field quality control in the Ocular Hypertension Treatment Study (OHTS). *J Glaucoma*. 2007;16:665-669.
 12. Zhou C, Qian S, Wu P, Qiu C. Quality of life of glaucoma patients in China: sociodemographic, clinical, and psychological correlates—a cross-sectional study. *Qual Life Res*. 2014;23:999-1008.
 13. Arora KS, Boland MV, Friedman DS, Jefferys JL, West SK, Ramulu PY. The Relationship between better-eye and integrated visual field mean deviation and visual disability. *Ophthalmology*. 2013;120:2476-2484.
 14. Nelson P, Aspinall P, Pappasoulitis O, Worton B, O'Brien C. Quality of life in glaucoma and its relationship with visual function. *J Glaucoma*. 2003;12:139-150.
 15. Khadka J, Pesudovs K, McAlinden C, Vogel M, Kernt M, Hirneiss C. Reengineering the glaucoma quality of life-15 questionnaire with rasch analysis. *Invest Ophthalmol Vis Sci*. 2011;52:6971-6977.
 16. Kowalski JW, Rentz AM, Walt JG, et al. Rasch analysis in the development of a simplified version of the national eye institute visual-function questionnaire-25 for utility estimation. *Qual Life Res*. 2012;21:323-334.
 17. Linacre JM. *A User's Guide to Winsteps/Ministeps Rasch-Model Programs*. Chicago, IL: MESA Press, 2005.
 18. Smith ND, Glen FC, Crabb DP. Eye movements during visual search in patients with glaucoma. *BMC Ophthalmol*. 2012;12:45.
 19. Khadka J, Gothwal VK, McAlinden C, Lamoureux EL, Pesudovs K. The importance of rating scales in measuring patient-reported outcomes. *Health Qual Life Outcomes*. 2012;10:80.
 20. McAlinden C, Skiadaresi E, Moore J, Pesudovs K. Subscale assessment of the NEI-RQL-42 questionnaire with Rasch analysis. *Invest Ophthalmol Vis Sci*. 2011;52:5685-5694.
 21. McAlinden C, Khadka J, de Freitas Santos Paranhos J, Schor P, Pesudovs K. Psychometric properties of the NEI-RQL-42 questionnaire in keratoconus. *Invest Ophthalmol Vis Sci*. 2012;53:7370-7374.
 22. McAlinden C, Jonsson M, Kugelberg M, Lundstrom M, Khadka J, Pesudovs K. Establishing levels of indications for cataract surgery: combining clinical and questionnaire data into a measure of cataract impact. *Invest Ophthalmol Vis Sci*. 2012;53:1095-1101.
 23. Gothwal VK, Wright TA, Lamoureux EL, Khadka J, McAlinden C, Pesudovs K. Improvements in visual ability with first-eye, second-eye, and bilateral cataract surgery measured with the visual symptoms and quality of life questionnaire. *J Cataract Refract Surg*. 2011;37:1208-1216.
 24. Mallinson T, Stelmack J, Velozo C. A comparison of the separation ratio and coefficient alpha in the creation of minimum item sets. *Med Care*. 2004;42:117-124.
 25. McAlinden C, Pesudovs K, Moore JE. The development of an instrument to measure quality of vision: the Quality of Vision (QoV) questionnaire. *Invest Ophthalmol Vis Sci*. 2010;51:5537-5545.
 26. McAlinden C, Skiadaresi E, Gatinel D, Cabot F, Huang J, Pesudovs K. The Quality of Vision questionnaire: subscale interchangeability. *Optom Vis Sci*. 2013;90:760-764.
 27. Linacre JM. Sample size and item calibration stability. *Rasch Meas Trans*. 1994;7:328.
 28. Skalicky SE, Goldberg I, McCluskey P. Ocular surface disease and quality of life in patients with glaucoma. *Am J Ophthalmol*. 2012;153:1-9.
 29. Skalicky SE, Martin KR, Fenwick E, Crowston JG, Goldberg I, McCluskey P. Cataract and quality of life in patients with glaucoma. *Clin Exp Ophthalmol*. 2015;43:335-341.
 30. Brabyn J, Schneck M, Haegerstrom-Portnoy G, Lott L. The Smith-Kettlewell Institute (SKD) longitudinal study of vision function and its impact among the elderly: an overview. *Optom Vis Sci*. 2001;78:264-269.
 31. Derefeldt G, Lennerstrand G, Lundh B. Age variations in normal human contrast sensitivity. *Acta Ophthalmol (Copenhagen)*. 1979;57:679-690.
 32. Boot WR, Stohart C, Charness N. Improving the safety of aging road users: a mini-review. *Gerontology*. 2014;60:90-96.
 33. Ekici F, Loh R, Waisbourd M, et al. Relationships between measures of the ability to perform vision-related activities, vision-related quality of life, and clinical findings in patients with glaucoma. *JAMA Ophthalmol*. 2015;133:1377-1385.
 34. Warrian KJ, Katz LJ, Myers JS, et al. A comparison of methods used to evaluate mobility performance in the visually impaired. *Br J Ophthalmol*. 2015;99:113-118.
 35. McKean-Cowdin R, Wang Y, Wu J, et al. Impact of visual field loss on health-related quality of life in glaucoma: the Los Angeles Latino Eye Study. *Ophthalmology*. 2008;115:941-948.