

Reliability and Construct Validity of the NEI VFQ-25 in a Subset of Patients With Geographic Atrophy From the Phase 2 Mahalo Study



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- **PURPOSE:** Geographic atrophy (GA) is an advanced form of age-related macular degeneration characterized by progressive, irreversible visual function loss. This analysis evaluates the psychometric properties of the 25-Item National Eye Institute Visual Function Questionnaire (NEI VFQ-25) composite, near activity, and distance activity scores in patients with GA.
- **DESIGN:** Reliability and validity study.
- **METHODS:** Reliability and validity were tested with NEI VFQ-25 data collected from 100 subjects with GA from United States' sites of the phase 2 Mahalo study of lampalizumab ([ClinicalTrials.gov](https://clinicaltrials.gov/ct2/show/study/NCT01229215) identifier: NCT01229215).
- **RESULTS:** Strong internal consistency and reproducibility were demonstrated for the NEI VFQ-25 composite (Cronbach's α , 0.95; intraclass correlation coefficient [ICC], 0.86), near activity (Cronbach's α , 0.84; ICC, 0.80), and distance activity (Cronbach's α , 0.84; ICC, 0.84) scores. Convergent validity with the binocular measures, Minnesota Low-Vision Reading Test (MNRead) reading speed and Functional Reading Independence (FRI) index score, was demonstrated for baseline NEI VFQ-25 composite (Pearson correlation [r] = 0.61 and 0.69, respectively), near activities (r = 0.69 and 0.73), and distance activities (r = 0.57 and 0.64) scores. Known-group validity testing for baseline mean NEI VFQ-25 scores (composite, near activities, and distance activities) showed differences between patients with mean maximum MNRead reading speed ≥ 80 vs < 80 words per minute, and between mean FRI index score ≥ 2.5 vs < 2.5 (all $P < .0001$).
- **CONCLUSIONS:** Psychometric evidence supports the NEI VFQ-25 as a reliable and valid cross-sectional measure of the impact of GA on patient visual function and vision-related quality of life. (*Am J Ophthalmol*

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GEOGRAPHIC ATROPHY (GA) IS AN ADVANCED form of age-related macular degeneration (AMD) estimated to affect more than 5 million people worldwide, including approximately 1 million people in the United States.^{1,2} It is a progressive and irreversible disease characterized by sharply delineated areas of atrophy of the retinal pigment epithelium, photoreceptors, and underlying choriocapillaris.^{3,4} As non-center-involving GA grows gradually over time, there can be profound impairments in visual function (eg, low-luminance visual acuity [LLVA], contrast sensitivity, and reading speed) owing to the presence of enlarging parafoveal scotomas, with minimal or no change in central visual acuity (VA).⁵ When the atrophic process involves the fovea, severe central vision loss can occur.⁶ Therefore, GA causes variable and often substantial effects on patients' visual function and vision-related quality of life (VRQoL) depending on the location and size of the GA.

Some patients with AMD report emotional distress and reduced quality of life (QoL)⁷ comparable to that reported among patients with advanced prostate cancer or severe cerebrovascular accident⁸ and worse than that reported among patients with chronic obstructive pulmonary disease or acquired immunodeficiency virus.⁷ In particular, patients with GA may report difficulties reading and recognizing faces even after accounting for their VA, have difficulty adapting to the dark, and may require additional light in order to read.⁵ Reading difficulties, a frequent complaint of patients with GA,^{9–11} can be an important indicator of VRQoL in those with macular disease involving central field loss.¹² Loss of central vision can be so debilitating that, among 1 cross-section of patients with end-stage AMD, many reported they would forfeit as much as half of their remaining life in return for healthy, normal vision.¹³

Currently, there is no treatment that prevents the development of GA in eyes with large drusen or that slows the worsening or growth of preexisting GA. In Report No. 35 from the Age-Related Eye Disease Study of patients with varying severity of AMD,¹⁴ a formulation containing the



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antioxidant vitamins C, E, and beta-carotene plus zinc did not reduce the incidence of progression to central GA over a 10-year follow-up period vs placebo. Ongoing clinical trials investigating multiple treatment pathways for GA include agents targeting complement and inflammation, the visual cycle, and neuroprotection, as well as cell replacement therapy.¹⁵ Combining an understanding of how these interventions may modify the GA disease process with patient-reported visual outcome measures could aid in understanding efficacy of new therapies from the patient's perspective.

A valid and convenient measure for assessing the impact of GA on visual function, in our opinion, remains an unmet need, as use of standard clinical tests of vision alone provide only a limited measure of visual performance in this condition.¹⁶ As outlined above, patients with GA may have good best-corrected visual acuity (BCVA) owing to central foveal preservation, but very poor function because of scotomas surrounding the fovea.⁵ Even when BCVA is impaired, standard objective testing may not capture the full impact of the disease from the perspective of the patient. Recently, the Functional Reading Independence (FRI) index,¹ a 7-item interviewer-administered questionnaire, was developed to assess the independence of patients with GA in performing activities of daily living that require reading. However, it does not capture broader aspects of visual function and VRQoL.

Use of the 25-Item National Eye Institute Visual Function Questionnaire (NEI VFQ-25)¹⁷ in GA may represent a viable option to better understand the impact of disease on a patient's day-to-day functioning and well-being. The NEI VFQ-25 is a patient-reported outcome (PRO) measure designed to assess the influence of visual impairment on vision-related function and multiple dimensions of VRQoL. This instrument has evidence of good psychometric properties, including reliability and construct validity, assessed using classical test theory in a mixed population of patients with various eye diseases and visual impairment.¹⁷

Although patients with AMD were included in the development and validation of the measure, the psychometric properties of the NEI VFQ-25 have not been documented in the specific context of use in patients with GA. The purpose of this analysis was to examine the psychometric properties of the NEI VFQ-25 in patients with GA who participated in a phase 2 clinical study of the anti-complement factor D therapy, lampalizumab. Emphasis was given to the reliability and validity of the NEI VFQ-25 composite score, near activity score, and distance activity score.

METHODS

• **STUDY DESIGN:** This reliability and validity study was a post hoc analysis of a multicenter, randomized, sham-controlled, phase 2 trial conducted in 129 subjects from

the United States and Germany to evaluate lampalizumab for GA secondary to AMD without choroidal neovascularization (Mahalo; [ClinicalTrials.gov](https://clinicaltrials.gov/ct2/show/study/NCT01229215) identifier: NCT01229215). Institutional review board and ethics committee approval was obtained prior to study initiation at each study site and all patients provided written informed consent. In Mahalo, subjects were randomized to 1 of 4 treatment arms, namely, intravitreal lampalizumab 10 mg or sham, administered monthly or every other month. The primary endpoint was mean change in GA lesion area from baseline to month 18.¹⁸ The NEI VFQ-25 was used as an exploratory outcome in the Mahalo trial.

• **MEASURES:** The analysis population was characterized using baseline demographics and clinical characteristics. Site personnel (other than the VA examiner) administered the NEI VFQ-25 in person at baseline and at 6, 12, and 18 months, or at early discontinuation from the study. The base questionnaire includes 25 items that comprise 11 subscales on different aspects of vision-related functioning and QoL and 1 item on general health.¹⁷ NEI VFQ-25 scores range from 0 to 100, with a higher score representing better functioning.¹⁷ Changes of 4-6 points have been judged to represent a clinically meaningful change, corresponding to a ≥ 15 -letter change in BCVA in patients with neovascular AMD.¹⁹ Given the importance of near and distance activities in patients with central vision loss,^{20,21} 6 additional NEI VFQ-25 Appendix items also were completed to enhance the reliability of the near and distance vision subscales (the NEI VFQ-25 with optional additional items is available at https://nei.nih.gov/sites/default/files/nei-pdfs/vfq_ia.pdf).²² The additional near-activity items included questions A3, A4, and A5 (pertaining to the level of difficulty in reading small print, figuring out bill accuracy, and performing everyday tasks), while the additional distance-activity items included questions A6, A7, and A8 (pertaining to the level of difficulty in recognizing familiar people from a distance, taking part in sports and other outdoor activities, and seeing/enjoying TV programs).²² Data from the following measures were collected at the same study time points as the NEI VFQ-25: GA lesion size (mm^2) as assessed by fundus autofluorescence (FAF) in the study eye; BCVA testing by the Early Treatment Diabetic Retinopathy Study (ETDRS) chart in the study eye; binocular Minnesota Low-Vision Reading test (MNRead: measures maximum reading speed, in words per minute [wpm]; chart consists of a series of simple sentences of fixed length, typically printed as black on white background, with systematically varying letter sizes)²³; and FRI index score.¹ The main results presented are for the composite, near, and distance activities subscales. The near activity and distance activity subscales have been shown to be important to patients with AMD, and are responsive to changes in BCVA in this patient group.^{19-21,24,25}

Complete results for the additional subscales (eg, driving, dependency) and other NEI VFQ-25 domains are

available online ([Supplemental Material](#) available at [AJO.com](#)).

- **ANALYSIS:** The present analysis included 100 subjects randomized from study sites in the United States with NEI VFQ-25 data at baseline from the 129 total subjects randomized. NEI VFQ-25 data collected in all 4 treatment arms were pooled to conduct the psychometric analysis, which was performed masked to treatment group assignment. All measures were scored according to the developers' guidelines, with no imputation conducted for missing values. Statistical tests involving multiple comparisons featured post hoc tests to adjust for multiple comparisons. SAS Version 9.4 (SAS Institute, Inc, Cary, North Carolina, USA) was used for all analyses.

- **STATISTICAL METHODS:** Internal consistency reliability of the NEI VFQ-25 was assessed using Cronbach's coefficient alpha to determine the extent to which individual items within each scale are related to each other and with the scale as a whole. Values range on an interval level scale from 0 to 1.0, with higher scores indicating a more reliable (homogeneous) instrument. Specifically, coefficients > 0.9 indicate high reliability suitable for evaluations of individual patients, and those between 0.7 and 0.9 indicate good internal consistency suitable for group comparisons.²⁶

Test-retest reliability of NEI VFQ-25 mean scores from baseline to month 6 was assessed by an intraclass correlation coefficient (ICC) within a prespecified subset of patients with little GA lesion growth ($n = 22$) based on a cut point of $\leq 0.45 \text{ mm}^2$ from baseline to 6 months. The cut point of 0.45 mm^2 is based on a study²⁷ (Schmitz-Valckenberg S, personal communication, September 2015) that assessed interobserver longitudinal measurement variability of novel semiautomated software for quantification of GA based on confocal scanning laser ophthalmoscopy FAF in 30 patients with GA. This value represents the mean difference in GA lesion size between 21 pairs of readers, plus twice the standard deviation of the interobserver difference for the 21 pairs of readers. To assess test-retest reliability, the ICC was calculated using a fixed-effects analysis of variance (ANOVA) model.²⁸ It was expected that the mean NEI VFQ-25 scores would not change across the retest interval. An ICC ≥ 0.7 indicates good test-retest reliability, 0.4-0.7 moderate, and < 0.4 low test-retest reliability.²⁹

Convergent validity (ie, the degree to which 2 measures theoretically expected to be related to each other are observed to be related to each other) was assessed by correlating baseline NEI VFQ-25 composite and subscale scores (Pearson correlations or Spearman rank correlations—depending on variable distributions) with MNRead reading speed, and the FRI index score. Correlation coefficients > 0.40 indicated acceptable convergent validity.³⁰ Stronger correlations were hypothesized between NEI VFQ-25 scores and the binocular measures

(ie, mean maximum MNRead reading speed and mean FRI index score) than with the monocular measures (ie, GA lesion size and BCVA ETDRS letter score) because subjective assessment of vision-dependent activities is associated more closely with binocular vision.^{12,31} A stronger relationship with monocular measures may be expected if the monocular measure was from the better-seeing eye, which was not usually the case in this study, in which the eye with the worse VA and/or least function was chosen as the study eye.³²

Known-groups validity reflects the capacity of the instrument to differentiate between groups known to be different based on another measure (eg, severity of symptoms).³³ To assess known-groups validity, subjects were stratified by GA lesion size (< 4 disc areas [$< 10 \text{ mm}^2$] and ≥ 4 disc areas [$\geq 10 \text{ mm}^2$] based on stratification criteria for randomization), BCVA ETDRS letter score ($>$ median and \leq median; baseline median 48 [approximate Snellen equivalent 20/125]), MNRead reading speed (≥ 80 wpm and < 80 wpm, where 80 wpm = minimally fluent reading),³⁴ and FRI index score (< 2.5 and ≥ 2.5 ; scores range from 1 to 4).

RESULTS

- **SAMPLE CHARACTERISTICS:** [Table 1](#) shows that patients in the analysis population were predominantly white (98%) and 60% were female, with a mean age of 79.7 years, and a median BCVA letter score of 48 (approximate Snellen equivalent: 20/125). Patients had impaired vision-specific functioning and VRQoL, as evidenced by a mean NEI VFQ-25 composite score of 61.7 at baseline, with driving (30.9) and near activities (48.4) the worst affected domains. Patients had a mean maximum MNRead reading speed of 104.7 wpm. The mean and median FRI index scores were in the middle of the 1- to 4-point range, indicating a moderate level of independence in performing daily activities that require reading.

- **INTERNAL CONSISTENCY AND TEST-RETEST RELIABILITY:** Baseline internal consistency assessment of the NEI VFQ-25 composite and subscales revealed high reliability of 0.95, 0.84, and 0.84 for composite score ($n = 30$), near activities ($n = 89$), and distance activities ($n = 63$), respectively. Good internal consistency was also demonstrated for dependency and driving (Cronbach's coefficient alpha = 0.79 and 0.75, respectively; [Supplemental Table 1](#), available at [AJO.com](#)). A total of 22 patients had $\leq 0.45 \text{ mm}^2$ GA lesion size growth from baseline to 6 months, thereby meeting the prespecified criteria for little GA lesion growth. The mean NEI VFQ-25 composite (ICC = 0.86), near activities (ICC = 0.80), and distance activities (ICC = 0.84) scores showed good test-retest reliability over 6 months in these patients ([Table 2](#)). ICC values also showed good reproducibility in other domains of the NEI VFQ-25 ([Supplemental Table 2](#), available at [AJO.com](#)).

TABLE 1. Baseline Characteristics of the 100 Patients With Geographic Atrophy Who Completed the 25-Item National Eye Institute Visual Function Questionnaire at Sites in the United States Participating in the Mahalo Study

| Parameter | Value |
|-------------------------------------------------------------|-------------------------------------|
| Demographics | |
| Mean age, years (SD) | 79.7 (7.1) |
| Women, n (%) | 60 (60.0) |
| White race, n (%) | 98 (98.0) |
| Vision-related clinical characteristics | |
| GA lesion size in mm ^{2a} | |
| Mean (SD) | 8.9 (4.5) |
| Median (range) | 8.3 (3-17) |
| Missing, n (%) | 18 (18.0) |
| BCVA letter score; approximate Snellen equivalent | |
| Mean (SD) | 48.0 (12.5); 20/125 |
| Median (range) | 48.0 (68-20); 20/125 (20/50-20/400) |
| Maximum MNRead reading speed, words per minute ^b | |
| Mean (SD) | 104.7 (61.1) |
| Median (range) | 82.3 (6-233) |
| Patient-reported outcome measure | |
| Mean FRI index ^c | |
| Mean (SD) | 2.5 (0.8) |
| Median (range) | 2.6 (1-4) |
| Mean NEI VFQ-25 score (SD) | |
| Composite score | 61.7 (16.3) |
| Near activities | 48.4 (21.7) |
| Distance activities | 56.1 (21.3) |
| Driving ^d | 30.9 (34.2) |
| General vision | 50.0 (18.1) |
| Mental health | 52.1 (25.5) |
| Role difficulties | 53.5 (25.5) |
| Dependency | 61.0 (30.8) |
| General health | 66.3 (19.6) |
| Social functioning | 71.0 (24.7) |
| Peripheral vision ^e | 74.7 (23.0) |
| Color vision ^f | 86.2 (19.7) |
| Ocular pain | 91.6 (15.5) |

BCVA = best-corrected visual acuity; FRI = Functional Reading Independence; GA = geographic atrophy; MNRead = Minnesota Low-Vision Reading Test; NEI VFQ-25 = 25-Item National Eye Institute Visual Function Questionnaire; SD = standard deviation.

^aN = 82; GA lesion size data included in this analysis were only for patients who completed month 18.

^bN = 95.

^cN = 94.

^dN = 89.

^eN = 99.

^fN = 98.

• **CONVERGENT VALIDITY:** As shown in Table 3, strong (0.60-0.79)³⁰ or moderate (0.40-0.59)³⁰ correlations were detected between baseline NEI VFQ-25 scores (composite,

near activities, and distance activities) and binocular maximum MNRead reading speed ($r = 0.61, 0.69,$ and 0.57 , respectively) and the FRI index score ($r = 0.69, 0.73,$ and 0.64 , respectively). Moderate or strong correlations were detected for some of the other NEI VFQ-25 domains, including driving score (Supplemental Table 3, available at [AJO.com](http://ajoo.com)). Weaker correlations were detected between these NEI VFQ-25 scores and the monocular measures of GA lesion size and BCVA ETDRS letter score, consistent with a priori expectations (Table 3).

Known-groups validity at baseline for the various categories of binocular and monocular measures is illustrated in the Figure. The mean maximum MNRead reading speed of ≥ 80 wpm was associated with higher NEI VFQ-25 scores than the mean maximum MNRead reading speed of < 80 wpm (composite: 68.8 vs 53.0; near activities: 60.1 vs 34.6; and distance activities: 64.6 vs 45.7; all $P < .0001$). A mean FRI index score of ≥ 2.5 was also associated with higher NEI VFQ-25 scores than a mean FRI index score of < 2.5 (composite: 69.8 vs 51.8; near activities: 61.0 vs 34.2; and distance activities: 66.7 vs 43.0; all $P < .0001$). Known-groups validity was not demonstrated for the monocular outcomes GA lesion size and BCVA, with the exception that a BCVA ETDRS letter score greater than the median of 48 (approximate Snellen equivalent: 20/125) was associated with a higher NEI VFQ-25 near activities score (53.2 vs 43.7; $P = .03$). Similar trends were detected for known-group validity at baseline for NEI VFQ-25 domain scores and the various categories of binocular and monocular measures, including the domains of driving and dependency, which were associated with the mean maximum MNRead reading speed and mean FRI index score (Supplemental Figure, available at [AJO.com](http://ajoo.com)).

DISCUSSION

THIS ANALYSIS FEATURED ESTABLISHED METHODOLOGY TO evaluate patient perception of vision-related functioning and vision-specific quality of life in a cross-sectional population with GA secondary to AMD who participated in the Mahalo clinical trial.^{17,22} The NEI VFQ-25 composite, near activities, and distance activities subscales demonstrated good internal consistency reliability, test-retest reliability, convergent validity, and known-groups validity with binocular measures of visual function (ie, binocular maximum reading speed and FRI index score). Although validation of the original 51-item NEI VFQ¹⁰ and NEI VFQ-25¹⁷ included patients with GA, these instruments have not been validated in a population with GA exclusively. Hence, this study goes beyond those reports to describe the convergent validity and reliability of the NEI VFQ-25 in patients with GA, and provides an opportunity to begin to characterize clinical and patient-centered outcomes in an era of emerging therapies for GA.

TABLE 2. Test-Retest Reliability of the NEI VFQ-25 in Patients With ≤ 0.45 mm² Geographic Atrophy Lesion Size Growth From Baseline to 6 Months

| Parameter | Composite Score (N = 22) | Near Activities (N = 22) | Distance Activities (N = 22) |
|-------------------------------------------------|--------------------------|--------------------------|------------------------------|
| Baseline, mean (SD) | 70.2 (15) | 60.0 (22) | 65.9 (20) |
| Month 6, mean (SD) | 71.0 (15) | 62.6 (21) | 66.9 (21) |
| Intraclass correlation coefficient ^a | 0.86 | 0.80 | 0.84 |

NEI VFQ-25 = 25-Item National Eye Institute Visual Function Questionnaire; SD = standard deviation.

^aValues > 0.70 indicate good test-retest reliability.

TABLE 3. Baseline Convergent Validity^a of the 25-Item National Eye Institute Visual Function Questionnaire With Binocular and Monocular Measures

| Measure | Composite Score (N = 82-100) | Near Activities (N = 82-100) | Distance Activities (N = 82-100) |
|------------------------------------|------------------------------|------------------------------|----------------------------------|
| Binocular measures | | | |
| Maximum MNRead reading speed (wpm) | 0.61 ^b | 0.69 ^b | 0.57 ^b |
| Mean FRI index | 0.69 ^b | 0.73 ^b | 0.64 ^b |
| Monocular measures | | | |
| GA lesion size (mm ²) | -0.25 ^c | -0.30 ^c | -0.23 ^c |
| BCVA testing (ETDRS letter score) | 0.15 | 0.27 ^c | 0.16 |

BCVA = best-corrected visual acuity; ETDRS = Early Treatment Diabetic Retinopathy Study; FRI = Functional Reading Independence; GA = geographic atrophy; MNRead = Minnesota Low-Vision Reading Test; wpm = words per minute.

^aConvergent validity assesses whether different measures of related concepts are correlated: values range from -1 to 1, with values >|0.30| indicating acceptable validity.

^bP < .0001 (Pearson correlation).

^cP < .05 (Pearson correlation).

The mean NEI VFQ-25 score of patients in this analysis was 61.7 (mean VA letter score [approximate Snellen equivalent]: 48.0 [20/125]). In previous trials, NEI VFQ-25 scores were 69.3 in MARINA (mean VA letter score [approximate Snellen equivalent]: 53.5 [20/80]) and 69.9 in ANCHOR (mean VA letter score [approximate Snellen equivalent]: 46.6 [20/125]) for patients with neovascular AMD,¹⁹ while in the Latino eye study composite NEI VFQ-25 scores were 59.5 for participants with advanced AMD, 79.4 for those with early AMD, and 80.7 in participants without AMD.³⁵ This suggests a degree of impaired visual functioning in this analysis population consistent with advanced AMD.

The NEI VFQ-25 composite, near activities, and distance activities scores had high internal consistency, indicating that items of the NEI VFQ-25 are highly related to each other and to the scale as a whole. Further, their high test-retest reliability reflects a capacity of the instrument to yield consistent results when GA lesion size growth is low (≤ 0.45 mm² over a 6-month period). Moderate or strong correlations for NEI VFQ-25 composite, near activities, and distance activities scores with maximum binocular MNRead reading speed and FRI index score were noted.³⁰

The good convergent validity of the NEI VFQ-25 in these patients provides evidence that this patient-centered tool represents the intended construct.^{33,36} Patients with higher mean maximum binocular MNRead reading speed or higher mean FRI index scores had higher NEI VFQ-25 composite, near activities, and distance activities scores, establishing known-groups validity in patients with GA. Other NEI VFQ-25 subscales, such as those for driving or dependency, also had acceptable internal consistency, test-retest reliability, convergent validity with binocular measures of visual function, and known-groups validity.

This study had some limitations that could affect the interpretation of the results. The small sample size of 100 patients limits interpretation of these findings, while the population included in this study may not be representative of the global population with GA. Additional research may be required to explore differences based on geography or ethnicity. In addition to the established drawbacks of post hoc subgroup analysis of exploratory endpoints (in this case the NEI VFQ-25), our evaluation of the psychometric properties of the NEI VFQ-25 was limited to the assessment of convergent validity and reliability using classical test theory. Item response theory (IRT) scores subjects

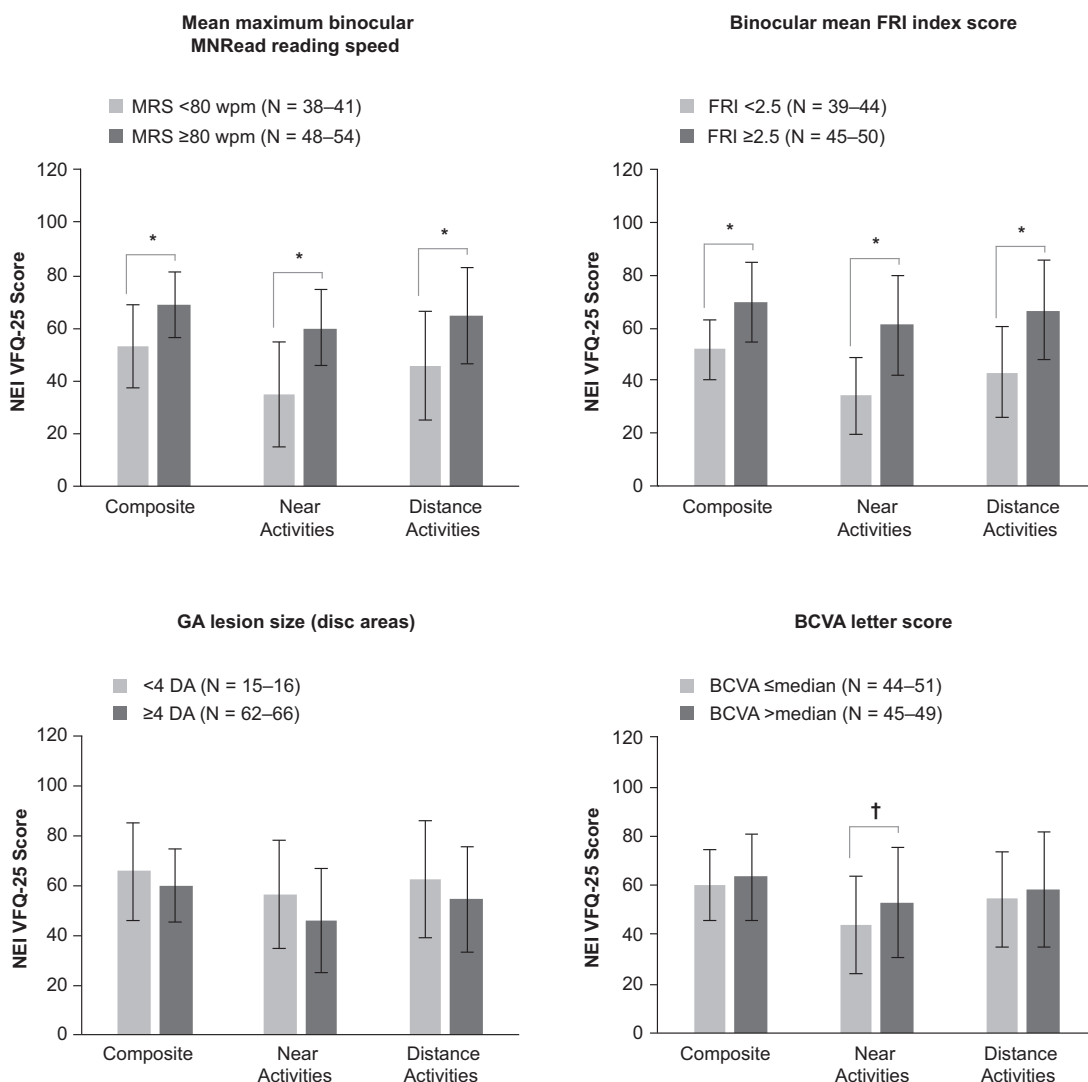


FIGURE. Known-groups validity of the 25-Item National Eye Institute Visual Function Questionnaire (NEI VFQ-25) at baseline with respect to: (Top left) maximum Minnesota Low-Vision Reading Test (MNRead) reading speed (< 80 and ≥80 words per minute [wpm]); (Top right) Functional Reading Independence (FRI) index score (< 2.5 and ≥2.5); (Bottom left) geographic atrophy (GA) lesion size (< 4 disc areas [$< 10 \text{ mm}^2$] and ≥4 disc areas [$\geq 10 \text{ mm}^2$]); and (Bottom right) median best-corrected visual acuity (BCVA) letter score (> 48.0 and ≤48.0). * $P < .0001$ analysis of variance (ANOVA). † $P = .03$ ANOVA. Error bars represent standard deviation. DA = disc areas; MRS = maximum MNRead reading speed.

on their abilities, attitudes, or other latent traits, and is used to calibrate and evaluate items in tests, questionnaires, and other instruments. IRT provides an alternate approach to the assessment of measurement properties, but was not applied in this analysis owing to insufficient sample size. Other measurement properties that were beyond the scope of this analysis but may be evaluated in the future are the factor structure of the NEI VFQ-25 in GA and the responsiveness of the NEI VFQ-25 in GA, particularly to changes or growth of GA over time. Finally, this analysis did not evaluate content validity of the NEI VFQ-25 in GA; however, supportive evidence of content validity of the NEI VFQ-25 in GA was recently documented in a qualitative study with 16 patients who had GA secondary to AMD

in the United States, United Kingdom, and Germany.³⁷ The results of that study indicated that the NEI VFQ-25 is generally considered clear and relevant, although some participants stated that some questions were repetitive.³⁷

This analysis potentially is relevant to clinical practice as it addresses a knowledge gap in the literature regarding the measurement of vision dysfunction and its consequences in patients with GA. At present, BCVA is used frequently to measure visual function performance in GA despite the caveat that the fovea is often preserved in affected patients until very late in the course of the condition,⁵ with limited information on a patient's perception and response to reduced vision among patients with GA. Findings of this study suggest the NEI VFQ-25 may have

value as a PRO in GA if changes in the NEI VFQ-25 are shown to be responsive to development or growth of GA.

To the best of our knowledge, the only other PRO questionnaire with evidence of validity and reliability in GA is the FRI index.¹ The NEI VFQ-25 captures different aspects of GA than the FRI index,¹ both of which can be viewed as complementary techniques that improve our understanding of visual disability in GA. Whereas the NEI VFQ-25 is a multidimensional instrument measuring

patient perception of vision-related function and vision-specific quality of life, the FRI index provides specific information on functional reading independence.¹

In conclusion, the psychometric evidence supports the use of the NEI VFQ-25 as a reliable and valid measure of the severe detrimental impact of GA on patients' visual function. Further research seems warranted with a larger sample size and with longitudinal data to evaluate the factor structure and responsiveness of the NEI VFQ-25 in GA.

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