Longitudinal Changes in Visual Acuity and Health-related Quality of Life

The Los Angeles Latino Eye Study

*Roberta McKean-Cowdin, PhD,[1] Rohit Varma, MD, MPH,[1,2] Ron D. Hays, PhD,[4,5,6] Joanne Wu, MS,[3] Farzana Choudhury, MS,[1] Stanley P. Azen, PhD,[1,2] and the Los Angeles Latino Eye Study Group**

Purpose: To examine the association between longitudinal changes in visual acuity (VA) and health-related quality of life (HRQOL) in a population-based sample of adult Latinos.

Design: A population-based cohort study of eye disease in Latinos.

Participants: We included 3169 adult Latino participants who live in the city of La Puente, California.

Methods: Data for these analyses were collected for the Los Angeles Latino Eye Study (LALES). Distance VA was measured during a detailed ophthalmologic examination using the standard Early Treatment Diabetic Retinopathy Study protocol at baseline and a 4-year follow-up examination. We assessed HRQOL by the National Eye Institute Visual Function Questionnaire (NEI-VFQ-25) and the Medical Outcomes Study 12-Item Short-Form Health Survey version 1 (SF-12).

Main Outcome Measures: Mean differences in HRQOL composite and subscale scores between baseline and follow-up were calculated for 3169 participants with complete clinical examination and HRQOL data at both time points. Mean differences and effect sizes (ES) for NEI-VFQ and SF-12 scores were calculated for 3 categories of VA change over the 4-year follow-up period (VA improved $\geq$2 lines, no change in VA or $-2 <$VA <2, VA loss $\geq$2 lines).

Results: For participants with a 2-line loss in VA, we noted an approximate 5-point loss in the NEI-VFQ-25 composite score, with the greatest score changes found for the driving difficulties, vision-related mental health, and vision-related dependency subscales (-12.7, -11.5, and -11.3, respectively). For participants with a 2-line improvement in VA, we also noted an approximate 5-point gain in the NEI-VFQ-25 composite score. The greatest change (ES = 0.80) was observed for the driving difficulties subscale. No measurable differences in HRQOL were observed for individuals without change in VA from baseline to follow-up.

Conclusions: Clinically important, longitudinal changes in VA ($\geq$2-line changes) were associated with significant changes in self-reported visual function and well-being. Both the size and direction of VA change influenced change in HRQOL scores.

Financial Disclosure(s): The authors have no proprietary or commercial interest in any of the materials discussed in this article. *Ophthalmology 2010;117:1900–1907*

**Group members of the Los Angeles Latino Eye Study Group listed online in Appendix 1 (available at http://aaojournal.org).*

Vision plays an important role in the ability of people to process information from their environment and to participate in many everyday activities such as reading, working at home or in the office, walking, driving, and interacting with others. People with visual impairment may face challenges completing these activities, which in some cases may lead to depression, social isolation, and difficulties at home, in school, or at work. We previously reported on significant associations between visual impairment, including visual acuity (VA) and visual field loss, and health-related quality of life (HRQOL) in the Los Angeles Latino Eye Study (LALES), a population-based study of adults (see Appendix 1; available at http://aaojournal.org).[1]

The National Eye Institute Visual Function Questionnaire (NEI-VFQ) was designed to measure areas of vision-targeted functioning and well-being that were identified as important by persons with eye disease.[2] Findings from previous studies[3–8] indicate that individuals with visual impairment have worse HRQOL than those without visual impairment. Using LALES cross-sectional data, a 2-line difference in presenting binocular VA was associated with a 5-point difference in the composite NEI-VFQ score.[9] In total, the findings from the literature suggest that early detection and appropriate treatment of visual impairment is important for maintenance of HRQOL. The analyses also indicate that the NEI-VFQ is sensitive enough to detect differences in HRQOL associated with clinically important differences in VA.

In the current analysis, we used longitudinal data to examine the association between changes in VA and changes in HRQOL over a 4-year follow-up period. We hypothesize, based on our earlier cross-sectional data, that

ISSN 0161-6420/10/$–see front matter
doi:10.1016/j.ophtha.2010.01.059

clinically meaningful improvements or losses in VA during the follow-up period would result in significant changes in HRQOL. Specifically, we wanted to determine if the association previously reported for cross-sectional data (a 2-line change in VA was associated with a 5-point change in HRQOL) was a reasonable indicator of the magnitude of the association for longitudinal data. Finally, we wanted to determine which NEI-VFQ subscale scores were most likely to be impacted by either worsening or improvement in VA and whether the magnitude of the changes mirrored each other (is a 2-line loss or improvement in VA associated with a similar change in HRQOL).

Methods

Data for these analyses were collected as part of a population-based study of eye disease in adults living in California. Details of the study design and data collected have been described previously.[1] We completed a census of all residential households in 6 census tracts in La Puente to identify individuals eligible to be included in the study. The definition of eligibility included men and women who were ≥40 years of age, self-described as Latino, and who lived in 1 of the 6 census tracts. Participants were given a verbal and written description of the study and invited to participate in both a home interview and a clinic examination between February 2000 and May 2003. A follow-up interview and clinical examination was completed approximately 4 years later (January 2004 through May 2008). Informed consent was completed with all participants before they participated in the clinical examination or questionnaire. All study procedures adhered to the principles outlined in the Declaration of Helsinki for research involving human subjects. Institutional review board ethics committee approval was obtained from the Los Angeles County/University of Southern California Medical Center Institutional Review Board (approval #969004 and 041004).

Sociodemographic and Clinical Data

An interview was completed at each participant's home that included information on demographics, history of medical conditions and eye diseases, access to health care, health insurance, vision insurance, and degree of acculturation.[10] Definitions were based on variables described in the Hispanic Health and Nutrition Examination Survey.[11,12] History of 12 medical conditions was asked and summarized using a comorbidity summation score that included diabetes mellitus, arthritis, stroke or brain hemorrhage, high blood pressure, angina, heart attack, heart failure, asthma, skin cancer, other cancers, back problems, and deafness or hearing problems.[13–15] Acculturation was measured using the short-form Cuellar Acculturation Scale, with scale scores ranging from 1 to 5 (5 representing the highest level of acculturation).[12]

Visual Acuity Testing

Measurement of distance VA in LALES has been described previously.[16–18] Presenting distance VA for each LALES participant was measured with the presenting correction (if any) at 4 meters using modified Early Treatment Diabetic Retinopathy Study distance charts transilluminated with the chart illuminator (Precision Vision, La Salle, IL). Presenting VA was scored as the total number of lines read correctly and converted to a logarithm of the minimum angle of resolution (logMAR) score. If a participant read <55 letters at 4 meters in either eye, an automated refraction (Humphrey Autorefractor model 509, Carl Zeiss Meditec, Dublin, CA) was performed. Those who subsequently read <55 letters while viewing through the prescription determined from the autorefractor underwent a subjective refraction using a standard protocol followed by a measurement of best-corrected VA. Testing began at the top of the chart and progressed to sequentially smaller lines (logMAR levels) provided 3 of 5 letters were identified correctly. When ≤2 letters were identified correctly, testing was discontinued. Best-corrected VA was defined as best VA measured at distance after subjective refraction was determined for each eye and was determined based on the person's better seeing eye. If a participant was unable to read 20 letters (20/100 Snellen) at 4 meters, VA measurement was performed at 1 meter.

Health-Related Quality of Life

Medical Outcomes Study 12-Item Short Form Health Survey. The Medical Outcomes Study 12-Item Short-Form Health Survey version 1 (SF-12)[19] was used to calculate the standard US, norm-based SF-12 Physical Component Summary (PCS) and Mental Component Summary (MCS) scores.[20] Higher PCS and MCS scores represent better HRQOL.[20] The PCS and MCS are scored on a T-score metric with the mean equal to 50 and SD equal to 10 in the general US population.

National Eye Institute Visual Function Questionnaire 5. Vision-targeted HRQOL was assessed by the NEI-VFQ-25.[2,21] This survey measures the influence of visual impairment and symptoms on generic health domains such as emotional well-being and social functioning, in addition to task-oriented domains related to daily visual functioning.[2,21] The survey is composed of 12 vision-targeted scales: General health (similar to one of the SF-12 items), general vision, near and distance vision activities, ocular pain, vision-related social function, vision-related role function, vision-related mental health, vision-related dependency, driving difficulties, color vision, and peripheral vision. Each scale consisted of a minimum of 1 and a maximum of 4 items. The standard recommended algorithm was used to calculate the scale scores, which have a possible range from 0 to 100. Higher scores represent better visual functioning and well-being. Eleven of the 12 scale scores (excluding the general health rating question) were averaged together to yield a composite score.[21]

Interviewers administered the questionnaires (before the clinical examination) in either English or Spanish at the LALES Local Eye Examination Center.

Statistical Analyses

Mean differences in HRQOL scores between baseline and follow-up examinations were calculated and tested for significance using a paired *t*-test ($P<0.05$). The proportion of participants who had ≥5 points differences in NEI-VFQ scores between the baseline and follow-up examinations were calculated.

Analysis of variance was used to compare the mean differences in HRQOL scores by 3 categories of VA change (VA improved ≥2 lines, no change in VA, VA loss ≥2 lines) for the best-corrected, better seeing eye and presenting, better seeing eye or both eyes. Effect sizes (ES) for NEI-VFQ scores were calculated for 3 categories of VA change for both presenting and the best-corrected, better seeing eye. The ES is an index used to measure the magnitude of impact of 1 variable on an outcome variable. To measure the impact of the magnitude of VA on HRQOL, ES was calculated as the difference in the mean scores between the baseline and follow-up examinations divided by the standard deviation (SD) of the scores for the baseline group.[22] Based on Cohen's suggestion, an ES of 0.20–0.49 is considered small, 0.50–0.79 moderate, and ≥0.80 or greater.[23,24]

To examine the possible nonlinear relationship between changes in VA and changes in HRQOL, predicted QOL values for NEI-VFQ scores were obtained through a regression model conditioned on an individual's change in VA (i.e., ≥2-line loss, <2-line change, ≥2-line improvement); models were adjusted for age, gender, education, employment status, income, acculturation, health insurance, vision insurance, number of comorbidities, visual field loss, and baseline VA. Predicted mean changes in NEI-VFQ-25 scores were plotted against change in VA for the best-corrected, better seeing eye. An iterative, locally weighted, least-squares method was used to generate lines of best fit (LOWESS fit line).[25]

The reliable change index (RCI) was calculated as a measure of the statistical significance of individual change in HRQOL. The RCI is a z test of change between baseline and follow-up, divided by the standard error of the difference.[26] An RCI beyond ±1.96 is indicative of reliable or statistically significant individual change at the $P<0.05$ level.

Analyses were conducted using SAS software 9.1 (SAS Inc., Cary, NC) at the 0.05 significance level. The LOWESS plots were created with STATA (STATA Corp, College Station, TX).

Results

Description of the Health-related Quality of Life Study Cohort

The HRQOL study cohort includes 3169 LALES participants with complete clinical examination and HRQOL data collected at baseline and at 4-years of follow-up. A total of 7789 participants were identified as eligible for LALES at baseline; 6142 (79%) had complete ophthalmic examination data and of these 4650 (76%) also had complete examination data at the 4-year follow-up examination. A total of 1192 participants were excluded from the analyses because they did not answer the NEI-VFQ-25 survey at 1 of the 2 time points, 222 were missing covariates, and an additional 67 participants were excluded because they did not answer the SF-12 on the baseline (n = 58) or follow-up (n = 9) questionnaires.

The majority of the LALES HRQOL study cohort is female (61%) with a mean age of 55 years at baseline and 1 to 2 chronic health conditions reported on average per person. Half the population reported they were employed at baseline (49.2%) with approximately 53% reporting they had vision insurance. Sixty-six percent of the population reported less than a high school education.

Changes in Visual Acuity and Health-related Quality of Life Scores from Baseline to Follow-up

Table 1 summarizes 4-year changes in VA and HRQOL scores from baseline to the 4-year follow-up examination. The LogMar VA score differences for presenting (binocular vision or better eye) and best corrected VA (better eye) indicate that mean VA became worse over the 4-year follow-up period. The mean difference was small, but significant. With respect to HRQOL scores, significant increases ($P<0.0001$) were found for 8 of 12 NEI-VFQ-25 scales and for the composite score ($P<0.0001$). A significant decrease in the NEI-VFQ-25 General Health score was found during the same time interval ($P<0.0001$). Consistent with this finding, the SF-12 PCS was significantly lower at follow-up than

Table 1. Difference between Mean Health-related Quality of Life Scores and Visual Acuity (VA) Logarithm of the Minimum Angle of Resolution (LogMar) Scores in the Los Angeles Latino Eye Study at the Baseline and 4-Year Follow-up Examinations (n = 3169)

	LALES I Mean (SD)	LALES II Mean (SD)	DIFF Mean (SD)	P-Value*	Proportion of Persons with ≥5 Points Change ↓	↑
NEI-VFQ 25						
Color vision	94.3 (14.8)	95.4 (13.6)	1.1 (16.4)	0.0002	9	12
Vision-related dependency	90.2 (19.2)	93.1 (19.2)	2.9 (20.1)	<0.0001	12	27
Driving difficulty†	88.4 (16.9)	88.2 (17.4)	−0.3 (16.3)	0.31	25	23
Distance vision	86.4 (18.0)	86.2 (18.3)	−0.1 (18.4)	0.65	26	29
General health	46.6 (22.9)	44.2 (22.9)	−2.3 (22.8)	<0.0001	27	19
General vision	68.9 (16.3)	69.5 (16.7)	0.6 (18.6)	0.09	25	27
Vision-related mental health	76.8 (21.2)	80.4 (20.9)	3.5 (21.8)	<0.0001	32	47
Near vision	80.1 (19.4)	82.3 (18.3)	2.2 (20.4)	<0.0001	34	40
Ocular pain	78.1 (20.2)	81.1 (18.9)	3.1 (20.7)	<0.0001	27	40
Peripheral vision	87.6 (20.1)	89.4 (18.8)	1.8 (21.3)	<0.0001	16	20
Vision-related role function	88.6 (20.7)	90.6 (19.3)	2.0 (21.9)	<0.0001	17	23
Vision-related social function	93.2 (13.8)	94.6 (12.7)	1.3 (15.0)	<0.0001	14	20
Composite score	84.2 (14.3)	86.1 (13.8)	1.9 (12.5)	<0.0001	20	32
SF12						
Physical composite score	46.4 (9.6)	45.9 (9.6)	−0.5 (9.3)	0.0015	25	22
Mental composite score	50.1 (10.7)	51.7 (10.6)	1.6 (11.3)	<0.0001	23	32
VA logMAR						
Presenting VA binocular	0.002 (0.148)	0.012 (0.168)	0.014 (0.141)	<0.0001	—	—
Presenting VA better eye	0.035 (0.154)	0.049 (0.171)	0.010 (0.134)	<0.0001	—	—
Best-corrected better eye	−0.019 (0.107)	−0.013 (0.131)	0.006 (0.093)	0.0006	—	—

DIFF = score difference between LALES II (4-year follow-up examination) and LALES I (baseline examination); LALES = Los Angeles Latino Eye Study; NEI-VFQ-25 = National Eye Institute Visual Function Questionnaire; SD = standard deviation; SF12 = Medical Outcomes Study 12-Item Short-Form Health Survey version 1.

*P-value is from the paired t-test.

†Score could be generated for only 2266 of the participants in the whole sample.

at baseline ($P = 0.0015$); however, the actual change was small. The SF-12 MCS was significantly higher ($P<0.0001$).

Change in Health-Related Quality of Life Stratified by Change in Visual Acuity

Table 2 presents mean changes in HRQOL and resulting ES by best-corrected VA change in the better seeing eye (VA improvement of ≥2 lines, no VA change, VA loss ≥2 lines) between LALES baseline and follow-up examinations. Although we also examined HRQOL differences for presenting VA of the better seeing eye, and for presenting VA for both eyes, the strongest associations were found for best corrected VA in the better seeing eye.

For participants with a 2-line loss in VA over the 4-year period based on best-corrected VA in the better seeing eye, we found an average 5.8-point loss in the NEI-VFQ-25 composite score (Table 2). Losses were greatest for driving difficulty (−12.7), vision-related mental health (−11.5), and vision-related dependency (−11.3). Small effects (ES = −0.20 to −0.49) were observed for 6 NEI-VFQ-25 subscales and the composite score. No measurable effect was found for the NEI-VFQ-25 general health scale or the SF-12 MCS or PCS.

For participants with a 2-line improvement in VA over the 4-year period based on best-corrected VA in the better seeing eye, we found an approximate 5-point gain in the NEI-VFQ-25 composite score. Small effects (ES = 0.20–0.49) were observed for 6 NEI-VFQ-25 subscales and the composite score. A large score change (25.0) and effect (ES = 0.80) was found for the driving subscale, suggesting that a ≥2-line improvement in VA had a strong, beneficial impact on participants' perception of their ability to drive independently. No measurable effect was found for the NEI-VFQ-25 general health scale or the SF-12 MCS or PCS. No measurable differences in HRQOL scores were observed for individuals without change in VA from LALES baseline to follow-up examinations.

For presenting VA in the better seeing eye or presenting VA based on both eyes, a ≥2-line loss in VA was associated with small effects for the NEI-VFQ-25 driving difficulty subscale. We observed a small effect for driving difficulty (ES = −0.28) when considering presenting VA in the better seeing eye and a small effect (ES = −0.43) when considering presenting VA in both eyes (data not shown). No effects were found among participants with minimal or no change in VA. For a 2-line improvement in presenting VA in the better seeing eye, small effects were found for 3 NEI-VFQ-25 subscales (vision-related mental health, near vision, ocular pain) and the composite score. For presenting VA based on both eyes, small effects were found for 9 of 12 subscales (color vision, vision-related dependency, distance vision, general vision, vision-related mental health, near vision, ocular pain, vision-related role function, and social function) and the composite score (data not shown). No effects were found for the SF-12 MCS or PCS for presenting VA in both eyes; a small effect was found for the MCS for participants with a ≥2-line loss for presenting VA in the better seeing eye (data not shown).

The RCI was used to evaluate the proportion of people with significant changes in NEI-VFQ-25 scores by VA change using the best corrected VA of the better seeing eye (Table 3; available online at http://aaojournal.org). For participants with a 2-line improvement in VA, the greatest proportions of people with significant improvements in HRQOL were found for ocular pain, driving difficulties, general vision, color vision, distance vision, peripheral

Table 2. Effect Size and Mean Change in Health-related Quality of Life (HRQOL) by Change in Best-corrected Visual Acuity (VA) of the Better Seeing Eye (n = 3169)

	Mean and Standard Deviation of the Difference in HRQOL Scores between LALES Baseline and Follow-up Examinations					
	VA Improved ≥ 2 Lines (n = 31)		*No VA Change (n = 3055)*		*VA Loss ≥ 2 Lines (n = 83)*	
	Mean (SD)	*ES*‡	*Mean (SD)*	*ES*‡	*Mean (SD)*	*ES*‡
NEI-VFQ-25						
Color vision*	8.6 (24.3)	0.39	1.2 (16.2)	0.08	−3.6 (21.1)	−0.19
Vision-related dependency*	1.3 (38.4)	0.04	3.3 (19.0)	0.18	−11.3 (37.5)	−0.41
Driving difficulty*†	25.0 (31.9)	0.80	−0.2 (15.7)	−0.01	−12.7 (29.6)	−0.42
Distance vision*	5.9 (30.5)	0.24	−0.05 (18.0)	−0.003	−4.9 (24.1)	−0.23
General health	−1.6 (26.9)	−0.07	−2.4 (22.6)	−0.11	−2.1 (25.6)	−0.09
General vision*	1.9 (18.6)	0.11	0.7 (18.5)	0.04	−5.6 (21.5)	−0.33
Vision-related mental health*	6.3 (30.4)	0.22	3.8 (21.4)	0.18	−11.5 (30.9)	−0.43
Near vision*	11.5 (20.1)	0.46	2.3 (20.3)	0.11	0.6 (24.8)	0.02
Ocular pain	8.6 (24.1)	0.30	3.1 (20.6)	0.16	1.6 (22.6)	0.07
Peripheral vision	−1.6 (32.3)	−0.07	1.9 (21.0)	0.10	−2.7 (26.6)	−0.11
Vision-related role function	−0.4 (31.2)	−0.01	2.1 (21.6)	0.10	−3.4 (28.9)	−0.11
Vision-related social function*	5.9 (24.0)	0.27	1.5 (14.5)	0.11	−6.3 (23.4)	−0.32
Composite score*	5.8 (18.3)	0.28	2.1 (12.2)	0.15	−5.9 (18.5)	−0.31
SF12						
Physical composite score	0.1 (10.0)	0.008	−0.6 (9.3)	−0.06	−0.6 (10.8)	−0.06
Mental composite score	3.1 (11.0)	0.22	1.6 (11.2)	0.15	0.6 (15.1)	0.05

ES = Effect size (small effect = 0.2–0.49; moderate effect = 0.50–0.79; large effect ≥ 0.80); HRQOL = health-related quality of life; NEI-VFQ-25 = National Eye Institute Visual Function Questionnaire; SD = standard deviation; VA = visual acuity; SF12 = Medical Outcomes Study 12-Item Short-Form Health Survey version 1.

*One-way analysis of variance, $P<0.05$.

†Score could be generated for only 2266 of the participants in the whole sample.

‡Effect size (ES) is defined as mean difference between LALES baseline and follow-up scores divided by standard deviation of baseline scores.

vision, and near vision (bolded in Table 3; available online at http://aaojournal.org). The scale with the smallest proportional improvement was vision-related social function. Cataract surgery was the reason for the 2-line improvement in VA for more than half of the participants with VA improvement. For participants with a ≥2-line loss, the largest proportion of people with significant loss in HRQOL were found for driving difficulty, general vision, peripheral vision, vision-related dependency, and vision-related mental health (bolded in Table 3; available online at http://aaojournal.org). The smallest proportional loss in HRQOL was found for the ocular pain scale.

Figures 1 and 2 show selected plots of predicted change in mean NEI-VFQ scores (composite scores, driving scores) by change in best-corrected VA of the better seeing eye. Plots of predicted change in mean NEI-VFQ composite scores show an approximate linear relationship with change in the best-corrected VA of the better seeing eye when considering data for a 2-line loss in VA through an approximate 4-line gain in VA (Fig 1); a more dramatic loss in composite scores was found for VA loss of ≥3 lines; however, these points were based on small numbers of participants. The same plot for the NEI-VFQ driving difficulty scale also shows an approximate linear relationship between change in driving scores and change in best-corrected VA for a 3-line loss in VA to a 2-line gain in VA; a greater change in NEI-VFQ driving scores was found for a VA gain of ≥3 lines or for a VA loss of ≥4 lines (Fig 2).

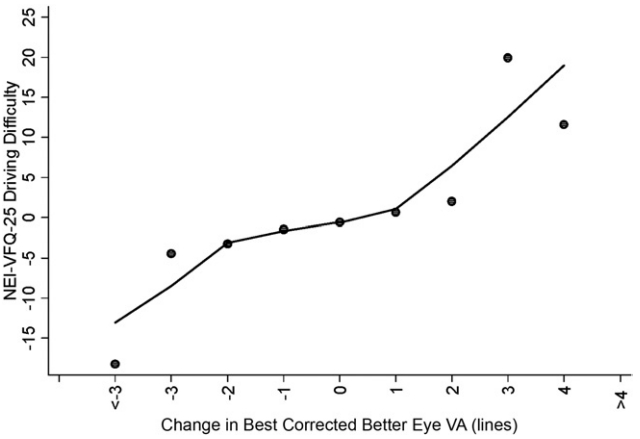

Figure 2. Linear regression plot of the relationship between change in the National Eye Institute Visual Function Questionnaire (NEI-VFQ-25) driving difficulty scores (adjusted for co-variates including age, gender, education, employment status, income, acculturation, comorbidities, health insurance, vision insurance, and baseline visual acuity [VA]) by change in best-corrected visual acuity in the better seeing eye of participants in the Los Angeles Latino Eye Study. The adjusted NEI-VFQ-25 composite scores were obtained using the regression model conditioned on VA status (vision loss, no change, vision improvement). The mean change in NEI-VFQ composite score of all participants by each unit of mean change in VA were plotted.

Discussion

In this population-based study of adults, we found statistically significant changes in mean HRQOL scores over the 4-year follow-up period for participants who had clinically meaningful changes in VA, although mean changes in HRQOL scores were small for participants with little or no change in VA.

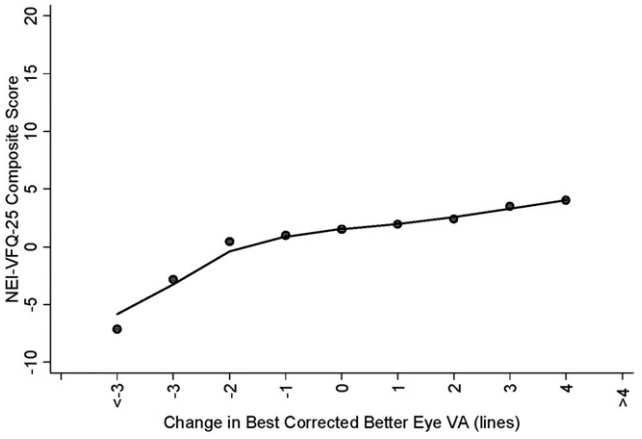

Figure 1. Linear regression plot of the relationship between change in the National Eye Institute Visual Function Questionnaire (NEI-VFQ-25) composite scores (adjusted for covariates including age, gender, education, employment status, income, acculturation, comorbidities, health insurance, vision insurance, and baseline visual acuity [VA]) by change in best-corrected VA in the better seeing eye of participants in the Los Angeles Latino Eye Study. The adjusted NEI-VFQ-25 composite scores were obtained using the regression model conditioned on VA status (vision loss, no change, vision improvement). The mean change in NEI-VFQ composite score of all participants by each unit of mean change in VA were plotted.

Several studies of clinic-based populations also have examined the relationships between longitudinal changes in VA and HRQOL. Mangione et al[5] found that improvements in VA after cataract surgery were associated with improvements in HRQOL as measured by the Activities of Daily Vision Scale (ADVS).[5] The participants included 419 cataract surgery patients aged ≥65 years with ADVS data available to assess changes in HRQOL after surgery. The ADVS includes 20 questions on visual activities related to 5 subscales: Night driving, daytime driving, distance vision activities, near vision activities, and glare.[27] Twelve months after cataract extraction, improvement in the best-corrected VA of the operated eye was associated with improvement in all 5 ADVS subscales after adjusting for VA of the nonoperated eye.

The Submacular Surgery Trials Research Group also found NEI-VFQ-25 scores were sensitive to changes in VA. The study included 828 patients from 3 clinical trials of submacular surgery for subfoveal choroidal neovascularization. Data on VA and NEI-VFQ-25 scores were collected at baseline (prerandomization) and 2 years postrandomization. The median age of the population was 75 years, approximately 20 years older than the LALES population. The best-corrected VA of each eye was measured. Investigators concluded that a 3-point difference in the NEI-VFQ-25 composite score and a 5.4-point difference in the driving difficulty score represented small but clinically meaningful changes when evaluating the VA data.[28,29] When restricting to patients with a ≥2-line improvement in VA of the better seeing eye, investigators found a mean NEI-VFQ-25 composite score change of 8.3 (SD = 12.8) and driving difficulty score change of 6.6 (SD = 24.4) over the 2-year interval. This improvement was greater than found in the

LALES population; however, their finding of a 5.9-point loss (SD = 17.4) in the NEI-VFQ-25 composite score for patients with a ≥2-line loss was the same as found in LALES. In general, mean changes in HRQOL scores for ≥2 line changes in VA for the clinical populations were greater than found for LALES.

The Age-Related Eye Disease Study Research Group also examined change in HRQOL with change in VA and found a ≥3-line loss in VA was associated with a 10-point change in the NEI-VFQ composite score. The sample for the VA analyses included 3624 people, aged 55 to 80 years at enrollment, identified from 11 clinical centers. Progression to VA loss was defined as a decrease of ≥3 lines between 2 NEI-VFQ-25 administrations at least 1 year and up to 4 years apart. The median age of the population was 72 years. The Age-Related Eye Disease Study Research Group found effects (ES) were moderate for 7 of 12 NEI-VFQ subscales and the composite score.

A 5-point change in NEI-VFQ measures has been suggested as a guideline for interpreting score differences as minimally important or as representing clinically meaningful change with respect to VA.[29] Several studies have examined the change in HRQOL scores for a 2- or 3-line change in VA. As mentioned, the Submacular Surgery Trials Research Group used the SD of change in NEI-VFQ scores from baseline to the 2-year follow-up examination to calculate a clinically meaningful change of the NEI-VFQ; score changes of 3.8 were considered small, 9.4 were considered medium, and 15 were considered large. In LALES, we chose to examine the change in HRQOL scores associated with a ≥2-line change in VA, because ≥2 lines is recognized as having clinical significance and is a level of change observed in the population. Clinical trial patients often achieve larger improvements in VA with treatment and therefore may achieve greater changes in HRQOL scores than can be expected when studying a general, population-based sample. Other differences that may influence the size of change in HRQOL scores between studies may include the baseline QOL score and the expectation of vision improvement after treatment by the patient.

We examined the proportion of individuals with significant changes in NEI-VFQ scores by change in VA using the RCI. A substantial proportion of individuals with clinically meaningful improvements or loss in VA had significant change in HRQOL scores. For example, 42% of individuals with a ≥2-line loss in VA over the 4-year follow-up period had a significant decline in the NEI-VFQ driving score. The proportion of individuals with significant changes in NEI-VFQ subscale scores was similar by direction of VA change (≥2-line gain vs ≥2-line loss) for many of the HRQOL subscales.

Small but significant losses in the general health measures (SF-12 PCS and NEI-VFQ general health scale) were found over the 4-year interval. These changes are likely due to additional health problems in this adult, aging population. The number of self-reported comorbidities from baseline to follow-up in our sample increased from an average 1.5 to 1.7. It is interesting that, despite the worsening of scores for the general health measures, the SF-12 MCS score improved significantly. After stratifying by change in VA status, we see that the small, positive change in the SF-12 MCS is attributable to the improvement in scores for the participants with a ≥2-line change in VA. The data suggest that improvements in vision after cataract surgery, glasses, or other clinical interventions are associated with gains in perceived well-being and function.

A limitation of the analyses is the small number of subjects with ≥2 lines of change in VA based on the best-corrected, better seeing eye. There were too few participants meeting these criteria to stratify by larger numbers of line changes (3 line changes, 4 line changes) and further explore the difference in HRQOL by line changes in VA. More participants reached a 2-line change based on presenting VA; however, the perceived impact of vision change in this group (whose vision could be corrected by refraction) was not as strong as in the best-corrected vision group. The plots showing change in NEI-VFQ scores by change in VA suggest a linear relationship through 2 to 3 lines of VA change; additional follow-up data are needed to accurately assess the shape of the relationship for larger changes in VA. Although strengths of this study are the collection of VA and visual field data over time, we do not have other longitudinal measures of vision such as contrast sensitivity. Additional strengths of the study include the population-based sample, the availability of both clinical and questionnaire data at 2 time points, and the collection of cataract history and use of glasses to allow for better interpretation of changes in HRQOL scores. The NEI-VFQ was scored using the standard methods based on classical test theory. However, increasing attention to applying item response theory methods in the evaluation and scoring of HRQOL measures is occurring.[30] Methodological research is needed to document the extent to which item response theory yields psychometric improvements to the NEI-VFQ and other HRQOL measures in future studies.[31]

In summary, clinically important changes in VA were associated with significant changes in HRQOL based on longitudinal data from a population-based sample of adults. The magnitude of the HRQOL effect was dependent on the size of the VA change and the direction of change (loss or gain in vision). A ≥2-line improvement in VA was associated with an average 5.8-point gain in the NEI-VFQ-25 composite score and a ≥2-line loss in VA was associated with an average 5.9-point loss. Previous studies have defined minimally important changes in HRQOL scores ranging from 3 to 5 points. The largest impact of VA change was found for the NEI-VFQ driving scale; a large effect (ES = 0.80) was found for individuals with a ≥2-line loss in VA. These data suggest that changes in a person's VA have a measurable and clinically important impact on perceived visual function and well-being.

References

1. Varma R, Paz SH, Azen SP, et al, Los Angeles Latino Eye Study Group. The Los Angeles Latino Eye Study: design, methods, and baseline data. Ophthalmology 2004;111: 1121–31.
2. Mangione CM, Lee PP, Pitts J, et al, NEI-VFQ Field Test Investigators. Psychometric properties of the National Eye

Institute Visual Function Questionnaire (NEI-VFQ). Arch Ophthalmol 1998;116:1496–504.
3. Submacular Surgery Trials Research Group. Health- and vision-related quality of life among patients with choroidal neovascularization secondary to age-related macular degeneration at enrollment in randomized trials of submacular surgery: SST report no. 4. Am J Ophthalmol 2004;138:91–108.
4. Linder M, Chang TS, Scott IU, et al. Validity of the Visual Function Index (VF-14) in patients with retinal disease. Arch Ophthalmol 1999;117:1611–6.
5. Mangione CM, Phillips RS, Lawrence MG, et al. Improved visual function and attenuation of declines in health-related quality of life after cataract extraction. Arch Ophthalmol 1994;112:1419–25.
6. Parrish RK II, Gedde SJ, Scott IU, et al. Visual function and quality of life among patients with glaucoma. Arch Ophthalmol 1997;115:1447–55.
7. Scott IU, Smiddy WE, Schiffman J, et al. Quality of life of low-vision patients and the impact of low-vision services. Am J Ophthalmol 1999;128:54–62.
8. Varma R, Wu J, Chong K, et al, Los Angeles Latino Eye Study Group. Impact of severity and bilaterality of visual impairment on health-related quality of life. Ophthalmology 2006;113:1846–53.
9. Globe DR, Wu J, Azen SP, Varma R, Los Angeles Latino Eye Study Group. The impact of visual impairment on self-reported visual functioning in Latinos: the Los Angeles Latino Eye Study. Ophthalmology 2004;111:1141–9.
10. Globe DR, Schoua-Glusberg A, Paz S, et al. Using focus groups to develop a culturally sensitive methodology for epidemiological surveys in a Latino population: findings from the Los Angeles Latino Eye Study (LALES). Ethn Dis 2002; 12:259–66.
11. Solis JM, Marks G, Garcia M, Shelton D. Acculturation, access to care, and use of preventive services by Hispanics: findings from HHANES 1982-84. Am J Public Health 1990; 80(suppl):11–9.
12. Marks G, Garcia M, Solis JM. Health risk behaviors of Hispanics in the United States: findings from HHANES, 1982–84. Am J Public Health 1990;80(suppl):20–6.
13. Brody BL, Gamst AC, Williams RA, et al. Depression, visual acuity, comorbidity, and disability associated with age-related macular degeneration. Ophthalmology 2001;108:1893–900; discussion 1900–1.
14. Linn BS, Linn MW, Gurel L. Cumulative illness rating scale. J Am Geriatr Soc 1968;16:622–6.
15. Globe DR, Varma R, Torres M, et al, Los Angeles Latino Eye Study Group. Self-reported comorbidities and visual function in a population-based study: the Los Angeles Latino Eye Study. Arch Ophthalmol 2005;123:815–21.
16. Azen SP, Varma R, Preston-Martin S, et al, Los Angeles Latino Eye Study Group. Binocular visual acuity summation and inhibition in an ocular epidemiological study: the Los Angeles Latino Eye Study. Invest Ophthalmol Vis Sci 2002; 43:1742–8.
17. Varma R, Fraser-Bell S, Tan S, et al, Los Angeles Latino Eye Study Group. Prevalence of age-related macular degeneration in Latinos: the Los Angeles Latino eye study. Ophthalmology 2004;111:1288–97.
18. Varma R, Torres M, Pena F, et al, Los Angeles Latino Eye Study Group. Prevalence of diabetic retinopathy in adult Latinos: the Los Angeles Latino eye study. Ophthalmology 2004;111:1298–306.
19. Ware J Jr, Kosinski M, Keller SD. A 12-item short-form health survey: construction of scales and preliminary tests of reliability and validity. Med Care 1996;34:220–33.
20. Ware JE Jr, Kosinski M, Keller SD. SF-12: How to Score the SF-12 Physical and Mental Health Summary Scales. 2nd ed. Boston: The Health Institute, New England Medical Center; 1995:41.
21. Mangione CM, Lee PP, Gutierrez PR, et al, National Eye Institute Visual Function Questionnaire Field Test Investigators. Development of the 25-item National Eye Institute Visual Function Questionnaire. Arch Ophthalmol 2001;119: 1050–8.
22. Rosenthal R. Parametric measures of effect size. In: Cooper HM, Hedges LV, eds. The Handbook of Research Synthesis. New York: Russell Sage Foundation; 1994:231–44.
23. Age-Related Eye Disease Study Research Group. Responsiveness of the National Eye Institute Visual Function Questionnaire to progression to advanced age-related macular degeneration, vision loss, and lens opacity: AREDS report no. 14. Arch Ophthalmol 2005;123:1207–14.
24. Cohen J. Statistical Power Analysis for the Behavioral Sciences. 2nd ed. Hillsdale, NJ: L. Erlbaum Associates: 1988:20–74.
25. Cleveland WS, Grosse E. Computational methods for local regression. Stat Comput 1991;1:47–62.
26. Hays RD, Brodsky M, Johnston MF, et al. Evaluating the statistical significance of health-related quality-of-life change in individual patients. Eval Health Prof 2005;28:160–71.
27. Mangione CM, Phillips RS, Seddon JM, et al. Development of the 'Activities of Daily Vision Scale': a measure of visual functional status. Med Care 1992;30:1111–26.
28. Submacular Surgery Trials Research Group. Evaluation of minimum clinically meaningful changes in scores on the National Eye Institute Visual Function Questionnaire (NEI-VFQ): SST report number 19. Ophthalmic Epidemiol 2007; 14:205–15.
29. Submacular Surgery Trials Research Group. Responsiveness of the National Eye Institute Visual Function Questionnaire to changes in visual acuity: findings in patients with subfoveal choroidal neovascularization—SST report no. 1. Arch Ophthalmol 2003;121:531–9.
30. Hays RD, Morales LS, Reise SP. Item response theory and health outcomes measurement in the 21st century. Med Care 2000;38(suppl):II28–42.
31. Reeve BB, Hays RD, Bjorner JB, et al, PROMIS Cooperative Group. Psychometric evaluation and calibration of health-related quality of life item banks: plans for the Patient-Reported Outcomes Measurement Information System (PROMIS). Med Care 2007;45(suppl):S22–31.

Footnotes and Financial Disclosures

Originally received: September 9, 2009.
Final revision: January 28, 2010.
Accepted: January 29, 2010.
Available online: June 8, 2010. Manuscript no. 2009-1241.

[1] Department of Preventive Medicine, Keck School of Medicine, University of Southern California, Los Angeles, CA.

[2] Department of Ophthalmology, Keck School of Medicine, University of Southern California, Los Angeles, CA.

[3] Titus Family Department of Clinical Pharmacy & Pharmaceutical Economics and Policy, School of Pharmacy, University of Southern California, Los Angeles, CA.

[4] Department of Health Services, UCLA School of Public Health, University of California at Los Angeles, Los Angeles, CA.

[5] Department of Medicine, Division of General Internal Medicine and Health Services Research, University of California at Los Angeles, Los Angeles, CA.

[6] RAND Corporation, Santa Monica, CA.

A list of the members of the Los Angeles Latino Eye Study Group is available online in Appendix 1 at http://aaojournal.org).

Financial Disclosure(s):
National Institutes of Health Grants NEI U10-EY-11753 and EY-03040 and an unrestricted grant from the Research to Prevent Blindness, New York, NY. Rohit Varma is a Research to Prevent Blindness Sybil B. Harrington Scholar. Ron D. Hays was supported in part by the UCLA Resource Center for Minority Aging Research/Center for Health Improvement in Minority Elderly (RCMAR/CHIME), NIH/NIA Grant Award Number P30AG021684.

Conflict of Interest: No conflicting relationship exists for any author.

Correspondence:
Rohit Varma MD, MPH, Doheny Eye Institute, 1450 San Pablo Street, Suite 4900, Los Angeles, CA 90033. E-mail: rvarma@usc.edu.

Table 3. Proportion of People with Significant Changes in National Eye Institute Visual Function Questionnaire-25 Scores for Individuals with ≥2 Line Changes in Best-corrected Visual Acuity (VA) of the Better Seeing Eye as Determined by the Reliable Change Index (RCI)

	Change in VA between Los Angeles Latino Eye Study Baseline and Follow-up Examinations			
	Increase 2 Lines VA (n = 31)		*Loss 2 Lines VA (n = 83)*	
NEI-VFQ-25	*Loss RCI≤−1.96 N (%)*	*Improvement RCI†≥1.96 N (%)*	*Loss RCI†≤−1.96 N (%)*	*Improvement RCI≥1.96 N (%)*
Color vision	4 (13)	**10 (32)**	21 (25)	13 (16)
Vision-related dependency	7 (23)	8 (26)	**26 (31)**	16 (19)
Driving difficulty	0 (0)	**3 (38)**	**16 (42)**	3 (8)
Distance vision	5 (16)	**10 (32)**	24 (29)	14 (17)
General health	11 (35)	8 (26)	22 (26)	14 (17)
General vision	7 (23)	**11 (35)**	**32 (39)**	17 (20)
Vision-related mental health	7 (23)	9 (29)	**26 (31)**	10 (12)
Near vision	2 (6)	**10 (32)**	14 (17)	16 (19)
Ocular pain	5 (16)	**12 (39)**	13 (16)	16 (19)
Peripheral vision	9 (29)	**10 (32)**	**27 (33)**	22 (27)
Vision-related role function	6 (19)	8 (26)	21 (25)	14 (17)
Vision-related social function	3 (10)	7 (23)	20 (24)	10 (12)
Composite score	6 (19)	**11 (36)**	**26 (31)**	12 (15)

LALES = Los Angeles Latino Eye Study; NEI-VFQ-25 = National Eye Institute Visual Function Questionnaire; VA = visual acuity.
Note: Percentage is for each line change group. For example, 31 participants increased 2 lines best-corrected better seeing eye visual acuity, 11 (11/31 = 35.48%) participants had RCI between ≤ −1.96 subscale general health.
†Bolded number and percent indicate those NEI-VFQ scores with a large (≥30%) percent of individuals with statistically significant change in score in the same direction as the direction of VA change.

Appendix 1. The Los Angeles Latino Eye Study Group (LALES I)

University of Southern California, Los Angeles, CA

Rohit Varma, MD, MPH; Sylvia H. Paz, MS; Stanley P. Azen, PhD; Lupe Cisneros, COA; Elizabeth Corona; Carolina Cuestas, OD; Denise R. Globe, PhD; Sora Hahn, MD; Mei-Ying Lai, MS; George Martinez; Susan Preston-Martin, PhD; Ronald E. Smith, MD; LaVina Tetrow, Mina Torres, MS; Natalia Uribe, OD; Jennifer Wong, MPH; Joanne Wu, MPH; Myrna Zuniga.

Battelle Survey Research Center, St. Louis, MO

Sonia Chico, BS; Lisa John, MSW; Michael Preciado, BA; Karen Tucker, MA.

Ocular Epidemiology Grading Center, University of Wisconsin, Madison, WI

Ronald Klein, MD, MPH.

The Los Angeles Latino Eye Study Group (LALES II)

University of Southern California, Los Angeles, CA

Rohit Varma, MD, MPH (Principal Investigator); Stanley P. Azen, PhD (Co–Principal Investigator); Mina Torres, MS (Project Director); Jaime Barrera; Farzana Choudhury, MBBS, MPH; Lupe Cisneros, COA; Jessica Chung, MPH, PhD; Elizabeth Corona; Carolina Cuestas, OD; Anne DiLauro, MPH (2005–2007); Jeanne Dzekov; Ana Evans (2004–2007); Athena W.P. Foong; Carlos Lastra, MD; Mei-Ying Lai, MS; George Martinez; Roberta McKean-Cowdin, PhD; Carlos Moya; Sylvia H. Paz, MS (2004–2005); Fernando Pena, MD (2004–2005); Corina Shtir, MS; Ronald E. Smith, MD; LaVina Tetrow (2004–2005); Heather Volk, PhD; Ying Wang, MS (2006–2007); Joanne Wu, MPH (2004-2006).

Battelle Survey Research Center, St. Louis, MO

Lisa John, MSW; Karen Tucker, MA; Natasha Van Leeuwen.

Ocular Epidemiology Grading Center, University of Wisconsin, Madison, WI

Ronald Klein, MD, MPH; Tiffany Jan; Michael D. Knudtson, MA; Stacy E. Meuer; Michael Neider.