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Progressive Visual Field Loss and Subsequent Quality of Life Outcomes in Glaucoma

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Abstract

Purpose: To evaluate the association between baseline severity of visual field(VF) damage and the initial rates of VF progression with quality of life(QOL) outcomes over an extended follow-up in glaucoma.

Design: Retrospective cohort.

Methods: Both eyes of 167 glaucoma or suspected glaucoma patients were followed for 10.0±0.3 years. The National Eye Institute Visual Function Questionnaire(NEI-VFQ)-25 was performed at the end of the follow-up. Separate linear regression models included the VF parameters of the better eye, the worse eye, and the central and peripheral points of the integrated binocular VF to evaluate the association of baseline and initial rates of change of VF parameters(first half of the follow-up) with NEI-VFQ-25 Rasch-calibrated disability scores over an extended follow-up.

Results: All models demonstrated association of worse baseline severity of VF damage with worse subsequent NEI-VFQ-25 scores. Faster rates of decline in VF mean deviation of the better eye and the mean sensitivity of the central and peripheral test locations of the integrated binocular VF were significantly associated with worse subsequent NEI-VFQ-25 scores. VF parameters of the better eye performed better than those of the worse eye(R^2 of 0.21, and 0.15, respectively), and

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the VF parameters of the central test locations performed better than those of the peripheral test locations (R^2 of 0.25, and 0.20, respectively).

Conclusions: Baseline severity and initial rates of change of VF damage are associated with QOL outcomes over an extended follow-up. Assessment of longitudinal VF changes, especially in better eye, provides prognostic utility to identify glaucoma patients at a higher risk for developing disease-related disability.

Graphical Abstract

This longitudinal study of glaucoma suspects and glaucoma patients found the baseline severity of visual field damage and its initial rate of progression as significant predictors of quality-of-life outcomes over an extended follow-up.

Keywords

Glaucoma; Quality of life; Visual field; 24-2; Longitudinal

Introduction

Glaucoma, a leading cause of worldwide blindness, is characterized by progressive retinal ganglion cell loss along with characteristic patterns of visual field (VF) damage.^{1,2} Glaucomatous damage reduces the patients' vision-related quality of life (QOL) with substantial impairments in multiple domains of everyday activities, including vision-dependent mobility and reading, and increases the risks of falls and motor vehicle collisions.³⁻⁹ Traditionally, VF damage in glaucoma is assessed by standard automated perimetry, with the 24-2 test being one of the most commonly used modalities. In contrast, the impact of glaucoma on vision-related QOL outcomes is generally evaluated by patient-reported questionnaires, such as the National Eye Institute Visual Function Questionnaire (NEI VFQ)-25.¹⁰⁻¹⁵

Several previous cross-sectional studies have provided insight into the relationship between the severity of VF damage and self-reported QOL outcomes in glaucoma patients.^{10,12,16-19} They have shown that higher severity of VF damage is associated with worse patient-reported QOL outcomes,¹⁰ and the strength of this association is stronger for the better eye's VF parameters compared to the worse eye.²⁰ It has also been suggested that the location of VF damage along with the overall severity needs to be considered to better assess the potential impact on QOL outcomes.^{21,22} This suggestion is motivated by prior findings that the 10-2 VF parameters provide a stronger association with NEI VFQ-25 scores compared to 24-2 VF parameters,²¹ and eyes with early glaucomatous macular damage have worse NEI VFQ-25 scores compared to those with arcuate damage outside the macular area.²²

Few prior longitudinal studies in glaucoma have investigated the influence of the rate of VF deterioration on patient-reported QOL outcomes.^{13,14,23} Lisboa and colleagues reported that faster VF progression within a follow-up is associated with a higher probability of reporting an abnormal vision-related QOL outcome at the end of that duration.¹³ Medeiros et al. found that both higher baseline severity and faster rates of VF progression are associated with a concurrent decline in the QOL of glaucoma patients.¹⁴ Also, a follow-up study revealed

that the previous associations are stronger for central locations of the VF than peripheral locations.²³

To our knowledge, no prior study has investigated the possible association between the initial rates of VF progression and future QOL outcomes of glaucoma patients over an extended follow-up duration. This information could provide substantial prognostic utility for risk assessment and clinical decision-making in glaucoma. For example, changes detected in the visual field, either in the better eye or worse eye, could provide an opportunity to initiate or escalate treatment to prevent QOL impairment. With that in mind, the principal aim of the present study was to investigate the association between the baseline severity of VF damage and the initial rates of VF progression with future NEI VFQ-25 disability scores over an extended follow-up duration.

Methods

Participants

This retrospective, longitudinal cohort study included all glaucoma suspect and glaucoma patients who were enrolled in the Diagnostic Innovations in Glaucoma Study (DIGS) and the African Descent and Glaucoma Evaluation Study (ADAGES) and met the inclusion criteria described below. DIGS and ADAGES were designed with similar testing protocols, and all participants were assessed longitudinally according to established protocols consisting of regular follow-up visits with clinical examination, imaging, and functional tests. The methodologic details of the mentioned studies have been described previously.^{24,25} Data analysis for the current study was conducted in June 2022, and written informed consent was obtained from all study participants. The University of California, San Diego Human Subject Committee approved all protocols, and the methods described adhered to tenets of the Declaration of Helsinki. Patients who participated in DIGS and ADAGES were compensated (\$50) for each of their twice-yearly visits.

All study participants underwent annual comprehensive ophthalmologic evaluation, including best-corrected visual acuity, slit lamp biomicroscopy, dilated fundus examination, and stereoscopic optic disc photography in both eyes. Semiannual evaluations included intraocular pressure (IOP) measurement and VF testing with Humphrey Field Analyzer 24-2 Swedish interactive thresholding algorithm standard test (Carl Zeiss Meditec, Inc., Dublin, CA, USA). This study included participants with longitudinal series of 24-2 VF tests starting 10 years prior to the NEI VFQ-25 assessment. A minimum of five VF tests/eye was required during the first half of the follow-up for each participant to calculate the initial rates of change of VF parameters.

Inclusion criteria at study entry also included (1) age older than 18 years, (2) open angles on gonioscopy, (3) best-corrected visual acuity of 20/40 or better, and (4) refraction plus or minus 5.0 diopters sphere and no more than 3.0 diopters cylinder. Exclusion criteria included (1) history of trauma or intraocular surgery (except for uncomplicated cataract or glaucoma surgery), (2) coexisting retinal disease, uveitis, or non-glaucomatous optic neuropathy, (3) other systemic or ocular diseases known to affect VF, such as pituitary

lesions or demyelinating diseases, (4) significant cognitive impairment; Parkinson disease, Alzheimer disease, dementia, or a history of stroke, or (5) axial length of 27 mm or more.

Glaucoma suspect eyes had either elevated IOP (≥ 22 mm Hg) or glaucomatous-appearing optic discs (glaucomatous optic neuropathy), without the presence of repeatable glaucomatous VF damage. Eyes classified as glaucomatous had repeatable (at least 2 consecutive) abnormal VF test results with evidence of glaucomatous optic neuropathy. Glaucomatous optic neuropathy was defined as excavation, the presence of focal thinning, notching of neuroretinal rim, or localized or diffused atrophy of the retinal nerve fiber layer, based on masked grading of optic disc photographs by 2 graders or clinical examination by a glaucoma specialist. An abnormal VF test result was defined as a pattern standard deviation (PSD) value at the 5% level or a glaucoma hemifield test result outside of normal limits.

Visual field testing

Visual field tests were performed using the Swedish Interactive Threshold Algorithm (SITA) standard 24-2 threshold test. All VFs were evaluated by the University of California, San Diego Visual Field Assessment Center personnel based on a standardized protocol.²⁴ Only reliable tests ($\leq 33\%$ fixation losses and false-negative errors, and $\leq 33\%$ false-positive errors) were included in the analysis. Visual fields with the following artifacts were also excluded: evidence of rim and eyelid artifacts, inattention or fatigue effects, or VF damage caused by a disease other than glaucoma such as homonymous hemianopia.

Separate models were developed to investigate the VF parameters' associations with end-of-follow-up Rasch-calibrated NEI VFQ-25 disability scores. The included VF parameters in each model were the baseline severity of VF damage and its initial rate of change during the first half of the follow-up. The models included the VF parameters of the better eye, the worse eye, the central integrated binocular test points, and the peripheral integrated binocular test points. The better and the worse eye of each participant was determined based on the 24-2 VF mean deviation (MD) at the baseline visit. For the central and peripheral points' comparison, an integrated binocular field was obtained using the monocular fields for the right and left eyes according to the binocular summation technique described by Nelson-Quigg et al.²⁶ After the binocular summation thresholds were obtained, the 52 thresholds points were divided into the central and peripheral regions, as shown in Figure 1. The central points were located in the region encompassing approximately the central 10° of the VF. Mean sensitivity (MS) in decibels (dB) was calculated for the central and peripheral regions by averaging the antilogs of the individual sensitivity thresholds and then recalculating the logarithm.

Rasch Analysis of NEI VFQ-25

The vision-related QOL was evaluated using the 25-item NEI VFQ. This questionnaire was designed to evaluate the dimensions of self-reported vision-related health status that are relevant for patients with chronic eye diseases, including glaucoma.^{27,28} The NEI VFQ consists of 25 vision-related questions that represent 11 subscales, with an additional single-item general health rating question. The 11 subscales are as follows: general vision, ocular pain, difficulty with near vision and distance activities, limitations with peripheral vision

and color vision, social functioning, driving difficulties, mental health symptoms related to vision, role limitations, and dependency. Each subscale consists of 1 to 4 items. Rasch analysis locates item difficulty and person ability on a logit scale. Person disability scores measured by the NEI VFQ were linearly rescaled ranging from 0 to 100 (eg, a score of 50 is equivalent to 50% of the worst disability score).^{29,30} The composite score or each subscale has a score of 100, representing the worst score on each item. Rasch analysis was conducted using Andrich rating scale models to acquire the estimates of the ability of each item, the perceived ability of each participant, and the category thresholds for each response category.^{14,31} Items belonging to mental health symptoms related to vision, role limitations, and dependency were excluded, as a previous study showed these items belong to a separate socioemotional dimension, not directly related to visual functioning.³² The NEI VFQ-25 assessment was conducted within 10±1 years after the baseline visit.

Demographic, Clinical, and Socioeconomic Variables

Demographic data, clinical, and socioeconomic questionnaires were obtained at the time of the NEI VFQ-25 assessment. These questionnaires contained a survey about demographics, educational level, income, marital status, and health insurance coverage. These variables were categorized to include in the multivariable models as educational level (at least a high school degree [yes/no]), income (<\$25,000 per year [yes/no]), marital status (married [yes/no]), and presence of health insurance (yes/no).¹³ Race was self-reported by the participants. For comorbidities, we accounted for the presence or history of the following conditions: arthritis, asthma, cancer, depression, diabetes, heart disease, hypertension, and stroke. A simple summation score was calculated as the comorbidity index score.³³

Statistical Analysis

Patient and eye characteristics data were presented as mean (95% CI) for continuous variables and count (%) for categorical variables. In separate models, the estimates of the rate of change in the metrics of VF damage for each eye were calculated by fitting an ordinary least squares linear regression method. The associations between the baseline severity of VF damage and its initial rate of change with the end of follow-up NEI VFQ-25 disability scores were evaluated using linear regression for each of the investigated models. The strength of the association and the statistical fit of the models were evaluated using the R^2 and Bayesian Information Criterion (BIC) metrics to compare the models' performance of the better eye versus the worse eye and the central integrated binocular test points to the peripheral integrated binocular test points. Statistical analyses were performed using Stata (version 17.0; StataCorp). The alpha level (type I error) was set at 0.05.

Results

This retrospective cohort study included 334 eyes (96 glaucoma suspect eyes, 238 glaucoma eyes) of 167 patients. The mean age at the initial VF visit was 64.3 years (62.8, 65.7). Seventy-three (43.7%) participants were male, and 78 (46.7%) of them had African-American ethnicity. The average MD and PSD of the participants at the initial VF visit were -1.7 dB (-2.2, -1.1), and 3.1 dB (2.6, 3.5) for the better eye and -5.4 dB (-6.4, -4.4), and 5.6 dB (4.9, 6.3) for the worse eye, respectively. As illustrated in Figure 2, baseline

MD values had a wide distribution range at the initial VF visit. The mean interval between the initial VF visit and the NEI VFQ-25 assessment was 10.0 years (9.9, 10.0). Study participants underwent an average of 9.8 (9.3, 10.3) VF tests per eye within the first half of this duration. The average NEI VFQ-25 disability scores at the end of the follow up was 45.8 (42.5, 49.2). Table 1 shows the summary characteristics of the study population.

In the univariable analysis, each 1 dB decline in the baseline better and worse eye MD values was associated with a corresponding 2.3-unit (1.5, 3.1, P -value < 0.001) and 1.2-unit (0.7, 1.7, P -value < 0.001) worse NEI VFQ-25 disability score, respectively. While each 1 dB/year faster initial rate of decline in the better eye MD was associated with a 13.5-unit (5.8, 21.3, P -value = 0.001) worse NEI VFQ-25 disability score, the association between the initial rate of change in the worse eye MD and the NEI VFQ-25 score was not statistically significant (2.8-unit worse score per each 1 dB/year faster rate of decline, -2.0, 7.7, P -value = 0.251) [Tables 2 and 3].

Both baseline MD (2.25-unit worse score/ 1 dB worse) and its initial rate of change (12.88-unit worse score/ 1 dB/year faster rate of decline) in the better eye were significantly associated with the NEI VFQ-25 disability score after concurrent inclusion in the same model (P -values < 0.001 for both variables). Figure 3 illustrates the contour plots of the estimated NEI VFQ-25 disability scores based on different levels of the better eye's baseline visual field (VF) mean deviation (MD) and its initial rate of change during the first half of the follow-up. The same analysis in the worse eye revealed a statistically significant association only for the baseline MD (2.25-unit worse score/ 1 dB worse), while the significance of the association of the initial rate of MD change with the NEI VFQ-25 disability score was borderline (3.93-unit worse score/ 1 dB/year faster rate of decline, P -value = 0.087). Compared to the worse eye ($R^2 = 0.15$), the combination of the baseline values and initial rates of MD change in the better eye ($R^2 = 0.21$) explained a higher percentage of variability and resulted in a strong improvement in the statistical fit of the model (BIC decrease = 11.74, BIC decrease of 6 is considered a strong model improvement³⁴) for the prediction of NEI VFQ-25 disability scores (Table 4).

After adjusting for the potential confounders, both worse baseline MD (2.0-unit worse score/ 1 dB worse, P -value < 0.001) and its faster initial rate of change (12.5-unit worse score/ 1 dB/year faster rate of decline, P -value = 0.003) in the better eye were significantly predictive of higher NEI VFQ-25 disability scores. The same analysis for the worse eye revealed a statistically significant association for the baseline MD (1.1-unit worse score/ 1 dB worse, P -value < 0.001); while the association for the initial rate of change did not reach statistical significance (3.7-unit worse score/ 1 dB/year faster rate of decline, P -value = 0.109). In addition to the VF parameters, the female gender and an annual income of lesser than \$25,000 were significantly associated with worse NEI VFQ-25 disability scores in both better-eye and worse-eye models (all P -values < 0.05). Tables 2 and 3 show the results of the multivariable analyses for the better and the worse eyes, respectively.

Table 5 illustrates the performance of the peripheral and the central binocular 24-2 VF test locations for the prediction of NEI VFQ-25 disability scores. Each 1-dB worse baseline MS was associated with worse NEI VFQ-25 disability scores of 3.58-unit (2.33, 4.82) for the

peripheral and 4.73-unit (3.33, 6.13) for the central VF locations, respectively. Similarly, each 1 dB/year faster rate of MS loss was associated with corresponding worse NEI VFQ-25 disability scores of 14.39-unit (4.93, 23.85) for the peripheral and 19.50-unit (9.18, 29.81) for the central VF locations (all P -values < 0.05). Compared to the peripheral points, the central VF test locations explained a higher percentage of variability of the NEI VFQ-25 disability scores (R^2 of 0.25 vs. 0.20) and resulted in a strong improvement in the statistical fit of the model (BIC decrease of 10.74).

Discussion

In this retrospective cohort study of glaucoma suspect and glaucoma patients, we demonstrated that the baseline severity of VF damage and the initial rates of VF progression are predictive of the future patient-reported QOL outcomes over an extended follow-up duration of almost a decade. Our findings highlight the significance of monitoring the eye with a better baseline functional status to preserve future QOL. We also showed that more central test locations of VF carry a greater influence on the future QOL outcomes than more peripheral areas. Our findings might have important clinical implications for identifying patients at risk of worse QOL outcomes in the future and for guiding the intensification of therapy based on the severity and rates of progression of VF damage in glaucoma.

The severity of baseline VF damage was a significant predictor of worse patient-reported QOL outcomes almost a decade in advance. In eyes with similar rates of VF progression, a 1-dB drop in the baseline MD of the better eye corresponded to a 2.25-unit worse NEI VFQ-25 disability scores, almost double the observed magnitude of the effect of the worse eye. It is helpful to clarify that the NEI VFQ-25 disability scores were scaled to range from 0 to 100, from the best reported in the study population to the worst one. Therefore, after adjusting for subsequent rates of VF progression in the better eyes (determined at baseline), an eye with a baseline MD of -10 dB (severe defect) had worse disability scores of up to 20% of the entire population scale compared to an eye with a baseline MD of -1 dB (mild defect). This observation highlights the importance of earlier identification of VF damage in glaucoma as further field loss in patients with already compromised vision is perhaps likely to affect more relevant areas for performing daily activities and thereby reduce patients' QOL.¹⁴

Several previous studies reported the association between the severity of VF damage and adverse QOL outcomes in glaucoma patients, with the majority having a cross-sectional design.^{10,16,19,35} Two subsequent population-based studies of the Los Angeles Latino Eye Study participants revealed worse patient-reported NEI VFQ-25 QOL outcomes even among patients with mild VF loss as determined by VF MD.^{10,19} It was interesting that this impact was present among the subgroup of participants who were previously unaware of their diagnosis, alleviating the potential concern of worse subjective interpretation of QOL outcomes as a consequence of disease recognition.¹⁰

The rate of VF progression is another major dimension of the risk assessment of glaucoma patients in terms of future vision-related QOL outcomes. It is reasonable to assume that among patients with similar magnitudes of VF damage, those with faster progression rates

have had less time to develop compensatory strategies and adjust their lifestyle accordingly and, therefore, are more likely to report a greater impact of VF damage on their perceived QOL.¹³ In fact, the validity of this hypothesis has been previously demonstrated in a few longitudinal studies. In a previous study of DIGS and ADAGES participants, Lisboa and colleagues reported that glaucoma patients have 30% greater odds of reporting an abnormal QOL outcome per each 0.1 dB/year faster history of binocular VF progression as determined within the entire follow-up duration.¹³ In a follow-up longitudinal study of DIGS participants, Medeiros et al. demonstrated that both baseline severity and the rates of change in bilateral VF MS as determined over the entire follow-up duration with an average of 3.5 years were significantly associated with worsening QOL outcomes in glaucoma patients.¹⁴ To our knowledge, this is the first longitudinal study to demonstrate that both baseline VF severity and the initial rates of VF worsening are significantly predictive of worse QOL outcomes over an extended follow-up period. After adjusting for baseline severity of VF damage and other potential confounders of QOL interpretation, each 1 dB/year faster rate of progression in the better eye with the first half of the follow-up was associated with worse QOL disability scores of up to 12.5% of the entire population scale. Depending on the availability of adequate information regarding the disease course, this finding should have significant clinical implications regarding risk assessment of glaucoma patients to determine the candidates for more intensive therapy.

Compared to the worse eye determined at baseline, the VF parameters of the better eye had a higher magnitude of effect on the QOL outcomes. Moreover, the model that included the VF parameters of the better eye explained a higher percentage of variability of the QOL outcomes and significantly improved the overall statistical fit. Consistently, prior studies support a closer relationship of the VF metrics of the better eye with measures of ability, performance, and QOL.^{20,36-42} However, the vast majority of this evidence comes from cross-sectional studies. In this regard, a previous study of more than 7500 glaucoma patients reported that better eye MD rarely differs from bilateral VF MD, and these two metrics provide similar associations with QOL scores.²⁰ In addition, easier interpretation and lack of need for extra calculations make better eye MD a robust and meaningful surrogate in clinical decision-making to assess the impact of VF damage on the QOL outcomes.²⁰ The present findings add further longitudinal evidence to highlight the prognostic significance of considering and monitoring the better eye's functional status with respect to subsequent QOL outcomes.

In addition to the global measures of VF damage, separate analyses indicated that damage in the central VF locations has a stronger association with subsequent QOL outcomes than peripheral locations. To compare the central and peripheral locations, integrated binocular VFs were used. It should also be noted that both worse baseline severity of damage and faster initial rates of progression in the central and peripheral VF locations were predictive of worse subsequent QOL disability scores. These simultaneous effects indicate the importance of both the baseline reserve and the necessary time to develop adequate compensatory strategies compared to the magnitude of VF damage when predicting future QOL outcomes based on longitudinal trends of VF damage in glaucoma patients. Our findings are in line with prior evidence on the importance of central VF damage on vision-related disability and QOL.^{21,23} A prior cross-sectional study in glaucoma patients with

concurrently available 10-2 and 24-2 VF tests demonstrated that the severity of damage on the 10-2 test grid shows a stronger association with NEI VFQ-25 scores compared to that of the 24-2 test. The authors also suggested that patients with disproportionately worse QOL scores than based on their magnitude of 24-2 VF damage might have undetected damage on the 10-2 test grid.²¹ Moreover, a longitudinal study of glaucoma patients with an average follow-up duration of 4.3 years demonstrated that both worse baseline severity and faster rate of VF progression in the central binocular 24-2 VF locations demonstrate a stronger association with simultaneous changes in patient-reported QOL outcomes compared to peripheral locations.²³

Our study has some limitations. Several prior studies have suggested that functional changes may not follow a linear trend over the course of glaucoma progression.^{43,44} However, a linear assumption to model the initial rates of VF progression is probably reasonable for short and intermediate follow-up periods, as conducted in clinical practice and used in the present study.¹⁴ Moreover, the assessment of QOL in glaucoma patients is a complex and multidimensional issue, and this task becomes more challenging when it is to be predicted in advance. The most commonly available methods for QOL evaluation, as the one used in this study are based on personal interpretation of difficulties in performing everyday tasks. Consequently, they are subject to variability based on personal values and expectations. A potential solution to address this limitation and a suitable direction for future investigations might be to assess the predictivity of VF parameters for the performance-based measures of disability. Additionally, long-term participants in DIGS and ADAGES may not reflect the general population seeking glaucoma care given the incentives provided and enhanced testing and follow-up involved. Lastly, since it is possible that more rapidly progressing and severe patients received different treatments, our study cannot access the mechanism of the relationship between VF severity, and progression and the final QOL outcomes independent of these treatment effects.

In conclusion, baseline severity of VF damage and its initial rates of change were significantly associated with future QOL outcomes over an extended follow-up duration. The VF parameters of the better eye and central locations of VF were associated with a higher magnitude of the effect regarding their impact on future QOL outcomes. Assessment of longitudinal VF changes, especially in the better eye, provides valuable prognostic information to identify glaucoma patients at a higher risk of vision-related QOL disability in whom intensification of therapy should be considered.

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Abbreviations and Acronyms:

ADAGES	African descent and glaucoma evaluation study
BIC	Bayesian information criterion
DIGS	diagnostic innovations in glaucoma study
IOP	intraocular pressure
MD	mean deviation
MS	mean sensitivity
NEI VFQ	national eye institute visual function questionnaire
PSD	pattern standard deviation
QOL	quality of life
SITA	Swedish Interactive Threshold Algorithm
VF	visual field

References

- Weinreb RN, Aung T, Medeiros FA. The pathophysiology and treatment of glaucoma: a review. *Jama*. May 14 2014;311(18):1901–11. doi:10.1001/jama.2014.3192 [PubMed: 24825645]
- Weinreb RN, Leung CK, Crowston JG, et al. Primary open-angle glaucoma. *Nature reviews Disease primers*. Sep 22 2016;2:16067. doi:10.1038/nrdp.2016.67
- Ramulu P. Glaucoma and disability: which tasks are affected, and at what stage of disease? *Curr Opin Ophthalmol*. Mar 2009;20(2):92–8. doi:10.1097/ICU.0b013e32832401a9 [PubMed: 19240541]
- Haymes SA, LeBlanc RP, Nicolela MT, Chiasson LA, Chauhan BC. Glaucoma and on-road driving performance. *Invest Ophthalmol Vis Sci*. Jul 2008;49(7):3035–41. doi:10.1167/iovs.07-1609 [PubMed: 18326696]
- Owsley C, McGwin G Jr. Vision and driving. *Vision Res*. Nov 23 2010;50(23):2348–61. doi:10.1016/j.visres.2010.05.021 [PubMed: 20580907]
- Ramulu PY, West SK, Munoz B, Jampel HD, Friedman DS. Glaucoma and reading speed: the Salisbury Eye Evaluation project. *Archives of ophthalmology (Chicago, Ill : 1960)*. Jan 2009;127(1):82–7. doi:10.1001/archophthalmol.2008.523 [PubMed: 19139345]
- Haymes SA, Leblanc RP, Nicolela MT, Chiasson LA, Chauhan BC. Risk of falls and motor vehicle collisions in glaucoma. *Invest Ophthalmol Vis Sci*. Mar 2007;48(3):1149–55. doi:10.1167/iovs.06-0886 [PubMed: 17325158]
- Skalicky SE, Goldberg I. Are we ready to assess quality of life routinely in our glaucoma patients? *Bull Soc Belge Ophthalmol*. 2010;(315):5–7.
- 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*. Jan 2009;18(1):6–12. doi:10.1097/IJG.0b013e3181752c83 [PubMed: 19142128]
- McKean-Cowdin R, Wang Y, Wu J, Azen SP, Varma R. Impact of visual field loss on health-related quality of life in glaucoma: the Los Angeles Latino Eye Study. *Ophthalmology*. Jun 2008;115(6):941–948.e1. doi:10.1016/j.ophtha.2007.08.037 [PubMed: 17997485]
- Spaeth G, Walt J, Keener J. Evaluation of quality of life for patients with glaucoma. *Am J Ophthalmol*. Jan 2006;141(1 Suppl):S3–14. doi:10.1016/j.ajo.2005.07.075 [PubMed: 16389055]

12. Jampel HD. Glaucoma patients' assessment of their visual function and quality of life. *Trans Am Ophthalmol Soc.* 2001;99:301–17. [PubMed: 11797316]
13. Lisboa R, Chun YS, Zangwill LM, et al. Association between rates of binocular visual field loss and vision-related quality of life in patients with glaucoma. *JAMA ophthalmology.* Apr 2013;131(4):486–94. doi:10.1001/jamaophthalmol.2013.2602 [PubMed: 23450425]
14. Medeiros FA, Gracitelli CP, Boer ER, Weinreb RN, Zangwill LM, Rosen PN. Longitudinal changes in quality of life and rates of progressive visual field loss in glaucoma patients. *Ophthalmology.* Feb 2015;122(2):293–301. doi:10.1016/j.ophtha.2014.08.014 [PubMed: 25444345]
15. Nishida T, Moghimi S, Mohammadzadeh V, et al. Association Between Ganglion Cell Complex Thinning and Vision-Related Quality of Life in Glaucoma. *JAMA ophthalmology.* Jun 30 2022;doi:10.1001/jamaophthalmol.2022.2140
16. van Gestel A, Webers CA, Beckers HJ, et al. The relationship between visual field loss in glaucoma and health-related quality-of-life. *Eye (London, England).* Dec 2010;24(12):1759–69. doi:10.1038/eye.2010.133 [PubMed: 21057519]
17. Gutierrez P, Wilson MR, Johnson C, et al. Influence of glaucomatous visual field loss on health-related quality of life. *Archives of ophthalmology (Chicago, Ill : 1960).* Jun 1997;115(6):777–84. doi:10.1001/archopht.1997.01100150779014 [PubMed: 9194730]
18. Parrish RK, Gedde SJ, Scott IU, et al. Visual function and quality of life among patients with glaucoma. *Archives of Ophthalmology.* 1997;115(11):1447–1455. [PubMed: 9366678]
19. McKean-Cowdin R, Varma R, Wu J, Hays RD, Azen SP. Severity of visual field loss and health-related quality of life. *Am J Ophthalmol.* Jun 2007;143(6):1013–23. doi:10.1016/j.ajo.2007.02.022 [PubMed: 17399676]
20. 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.* Dec 2013;120(12):2476–2484. doi:10.1016/j.ophtha.2013.07.020 [PubMed: 23993358]
21. Blumberg DM, De Moraes CG, Prager AJ, et al. Association Between Undetected 10-2 Visual Field Damage and Vision-Related Quality of Life in Patients With Glaucoma. *JAMA ophthalmology.* Jul 1 2017;135(7):742–747. doi:10.1001/jamaophthalmol.2017.1396 [PubMed: 28542692]
22. Garg A, Hood DC, Pensec N, Liebmann JM, Blumberg DM. Macular Damage, as Determined by Structure-Function Staging, Is Associated With Worse Vision-related Quality of Life in Early Glaucoma. *Am J Ophthalmol.* Oct 2018;194:88–94. doi:10.1016/j.ajo.2018.07.011 [PubMed: 30053467]
23. Abe RY, Diniz-Filho A, Costa VP, Gracitelli CP, Baig S, Medeiros FA. The Impact of Location of Progressive Visual Field Loss on Longitudinal Changes in Quality of Life of Patients with Glaucoma. *Ophthalmology.* Mar 2016;123(3):552–7. doi:10.1016/j.ophtha.2015.10.046 [PubMed: 26704883]
24. Sample PA, Girkin CA, Zangwill LM, et al. The African Descent and Glaucoma Evaluation Study (ADAGES): design and baseline data. *Archives of ophthalmology (Chicago, Ill : 1960).* Sep 2009;127(9):1136–45. doi:10.1001/archophthalmol.2009.187 [PubMed: 19752422]
25. Racette L, Liebmann JM, Girkin CA, et al. African Descent and Glaucoma Evaluation Study (ADAGES): III. Ancestry differences in visual function in healthy eyes. *Archives of ophthalmology (Chicago, Ill : 1960).* May 2010;128(5):551–9. doi:10.1001/archophthalmol.2010.58 [PubMed: 20457975]
26. Nelson-Quigg JM, Cello K, Johnson CA. Predicting binocular visual field sensitivity from monocular visual field results. *Invest Ophthalmol Vis Sci.* Jul 2000;41(8):2212–21. [PubMed: 10892865]
27. Mangione CM, Lee PP, Gutierrez PR, Spritzer K, Berry S, Hays RD. Development of the 25-item National Eye Institute Visual Function Questionnaire. *Archives of ophthalmology (Chicago, Ill : 1960).* Jul 2001;119(7):1050–8. doi:10.1001/archopht.119.7.1050 [PubMed: 11448327]
28. Mangione CM, Lee PP, Pitts J, Gutierrez P, Berry S, Hays RD. Psychometric properties of the National Eye Institute Visual Function Questionnaire (NEI-VFQ). NEI-VFQ Field Test

- Investigators. *Archives of ophthalmology* (Chicago, Ill : 1960). Nov 1998;116(11):1496–504. doi:10.1001/archophth.116.11.1496 [PubMed: 9823352]
29. Boone WJ, Staver JR, Yale MS. *Rasch analysis in the human sciences*. Springer; 2013.
 30. Bond TG, Fox CM. *Applying the Rasch model: Fundamental measurement in the human sciences*. Psychology Press; 2013.
 31. Andrich D. Rating scales and Rasch measurement. *Expert Rev Pharmacoecon Outcomes Res*. Oct 2011;11(5):571–85. doi:10.1586/erp.11.59 [PubMed: 21958102]
 32. Marella M, Pesudovs K, Keeffe JE, O'Connor PM, Rees G, Lamoureux EL. The psychometric validity of the NEI VFQ-25 for use in a low-vision population. *Invest Ophthalmol Vis Sci*. Jun 2010;51(6):2878–84. doi:10.1167/iovs.09-4494 [PubMed: 20089878]
 33. Globe DR, Varma R, Torres M, Wu J, Klein R, Azen SP. Self-reported comorbidities and visual function in a population-based study: the Los Angeles Latino Eye Study. *Archives of ophthalmology* (Chicago, Ill : 1960). Jun 2005;123(6):815–21. doi:10.1001/archophth.123.6.815 [PubMed: 15955983]
 34. Kass RE, Raftery AE. Bayes factors. *Journal of the american statistical association*. 1995;90(430):773–795.
 35. Jampel HD, Friedman DS, Quigley H, Miller R. Correlation of the binocular visual field with patient assessment of vision. *Invest Ophthalmol Vis Sci*. Apr 2002;43(4):1059–67. [PubMed: 11923247]
 36. Ramulu PY, West SK, Munoz B, Jampel HD, Friedman DS. Driving cessation and driving limitation in glaucoma: the Salisbury Eye Evaluation Project. *Ophthalmology*. Oct 2009;116(10):1846–53. doi:10.1016/j.ophtha.2009.03.033 [PubMed: 19592110]
 37. Nah YS, Seong GJ, Kim CY. Visual function and quality of life in Korean patients with glaucoma. *Korean J Ophthalmol*. Dec 2002;16(2):70–4. doi:10.3341/kjo.2002.16.2.70 [PubMed: 12546442]
 38. Kotecha A, O'Leary N, Melmoth D, Grant S, Crabb DP. The functional consequences of glaucoma for eye-hand coordination. *Invest Ophthalmol Vis Sci*. Jan 2009;50(1):203–13. doi:10.1167/iovs.08-2496 [PubMed: 18806294]
 39. Warrian KJ, Lorenzana LL, Lankaranian D, Dugar J, Wizov SS, Spaeth GL. The assessment of disability related to vision performance-based measure in diabetic retinopathy. *Am J Ophthalmol*. May 2010;149(5):852–60.e1. doi:10.1016/j.ajo.2009.12.028 [PubMed: 20399929]
 40. McGwin G Jr., Xie A, Mays A, et al. Visual field defects and the risk of motor vehicle collisions among patients with glaucoma. *Invest Ophthalmol Vis Sci*. Dec 2005;46(12):4437–41. doi:10.1167/iovs.05-0750 [PubMed: 16303931]
 41. Sumi I, Shirato S, Matsumoto S, Araie M. The relationship between visual disability and visual field in patients with glaucoma. *Ophthalmology*. Feb 2003;110(2):332–9. doi:10.1016/s0161-6420(02)01742-6 [PubMed: 12578777]
 42. Friedman DS, Freeman E, Munoz B, Jampel HD, West SK. Glaucoma and mobility performance: the Salisbury Eye Evaluation Project. *Ophthalmology*. Dec 2007;114(12):2232–7. doi:10.1016/j.ophtha.2007.02.001 [PubMed: 17980433]
 43. Hood DC, Kardon RH. A framework for comparing structural and functional measures of glaucomatous damage. *Prog Retin Eye Res*. Nov 2007;26(6):688–710. doi:10.1016/j.preteyeres.2007.08.001 [PubMed: 17889587]
 44. Medeiros FA, Zangwill LM, Bowd C, Mansouri K, Weinreb RN. The structure and function relationship in glaucoma: implications for detection of progression and measurement of rates of change. *Invest Ophthalmol Vis Sci*. Oct 5 2012;53(11):6939–46. doi:10.1167/iovs.12-10345 [PubMed: 22893677]

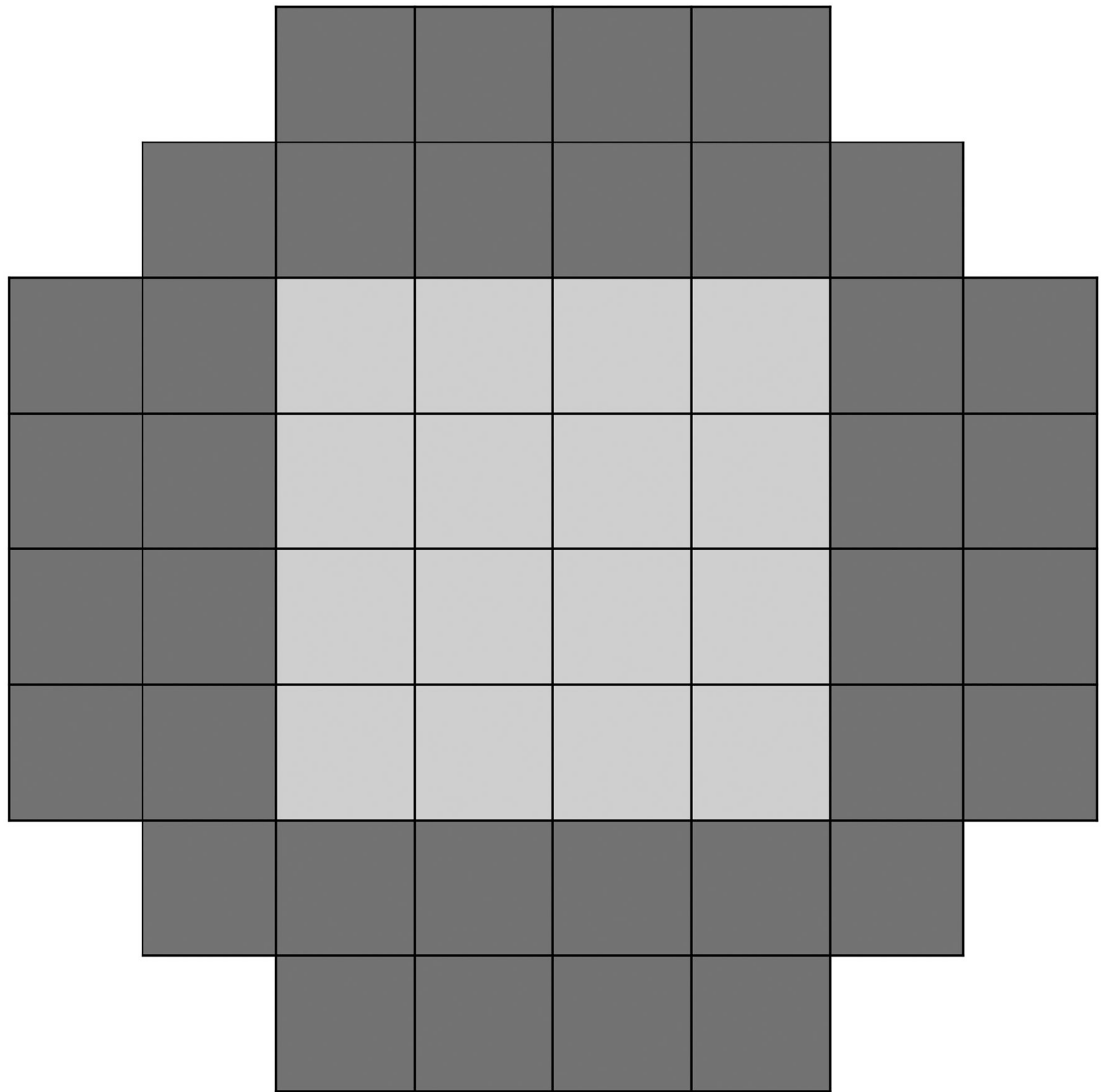


Figure 1. The binocular integrated visual field test points as divided into the central (light) and peripheral (dark) regions.

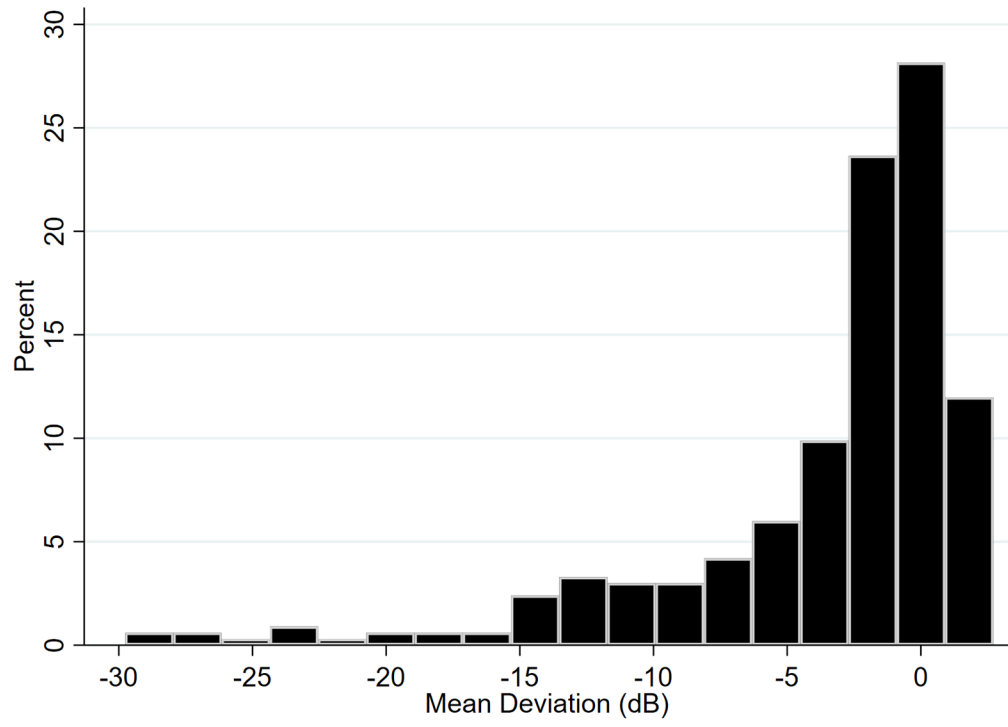


Figure 2. Distribution of baseline mean deviation values for all visual fields included in the study. dB = decibel.

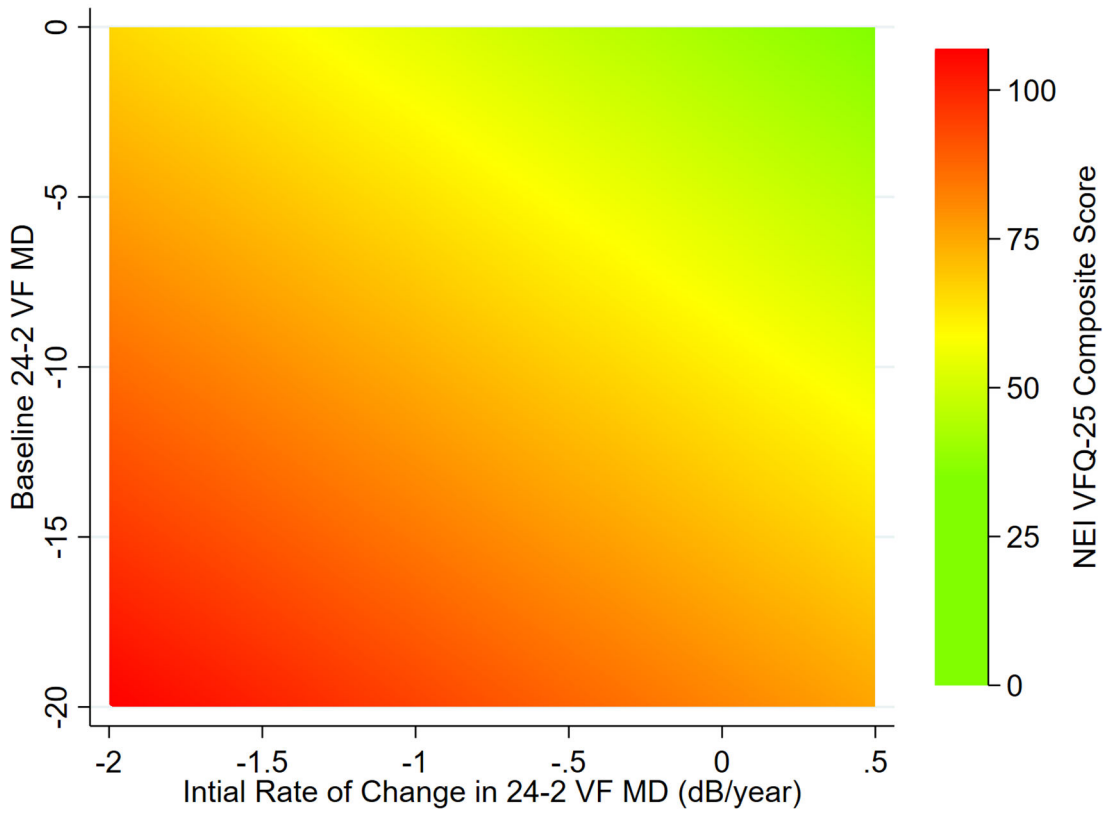


Figure 3. Contour plots showing the estimated National Eye Institute Visual Function Questionnaire (NEI VFQ)-25 disability scores based on different levels of the better eye’s baseline visual field (VF) mean deviation (MD) and its initial rate of change during the first half of the follow-up. Warmer colors represent higher estimated NEI VFQ-25 disability scores at the end of the follow-up. dB = decibel.

Table 1.

Baseline Clinical and Demographic Characteristics of the Study Population (n = 167)

Characteristic	Value
Patient-level	
Age at the baseline 24-2 VF visit, years	64.3 (62.8, 65.7)
Gender, % female	56.3
Race, % African American	46.7
Education level, % with at least a high school degree	96.4
Income, % <\$25000	10.8
Marital status, % married	47.3
Comorbidity index	2.1 (1.9, 2.3)
Insurance, % yes	99.4
Average initial follow-up duration with 24-2 VF test, years	4.9 (4.9, 5.0)
Average interval between the first 24-2 VF visit and NEI VFQ-25 test	10.0 (9.9, 10.0)
Eye-level	
LogMAR visual acuity (better eye)	0.03 (0.02, 0.05)
LogMAR visual acuity (worse eye)	0.06 (0.04, 0.08)
Baseline 24-2 MD (better eye), dB	-1.7 (-2.2, -1.1)
Baseline 24-2 MD (worse eye), dB	-5.4 (-6.4, -4.4)
Baseline 24-2 PSD (better eye), dB	3.1 (2.6, 3.5)
Baseline 24-2 PSD (worse eye), dB	5.6 (4.9, 6.3)
Initial 24-2 MD rate of change (better eye), dB/year	-0.16 (-0.23, -0.10)
Initial 24-2 MD rate of change (worse eye), dB/year	-0.23 (-0.34, -0.13)
History of glaucoma filtering surgery (better eye), % yes	11.4
History of glaucoma filtering surgery (worse eye), % yes	21.6
Average 24-2 VF tests	9.8 (9.3, 10.3)

NEI: national eye institute, VFQ-25: 25-item visual function questionnaire, LogMAR: logarithm of the minimum angle of resolution, MD: mean deviation, PSD: pattern standard deviation.

Values are represented as mean (95% confidence interval) unless otherwise noted.

Table 2.

Results of the Univariable and Multivariable Regression Models for the Association between Baseline and Initial Rates of Change in 24-2 Visual Field Mean Deviation of the Better Eye and National Eye Institute Visual Function Questionnaire-25 Score (n = 167)

Characteristic	Univariable Model		Multivariable Model	
	Coefficient	<i>P</i> -value*	Coefficient	<i>P</i> -value*
Age, per decade older	2.1 (-1.4, 5.6)	0.236	-0.2 (-3.9, 3.6)	0.926
Gender, female	8.5 (1.9, 15.1)	0.012	8.1 (1.1, 15.1)	0.025
Race, African American	3.7 (-3.0, 10.4)	0.275	1.6 (-4.9, 8.1)	0.628
Education level, at least high school degree	-11.2 (-29.2, 6.8)	0.221	-10.5 (-27.3, 6.4)	0.223
Income, <\$25000	17.4 (6.4, 28.4)	0.002	15.3 (4.9, 25.6)	0.004
Marital status, married	-1.4 (-8.1, 5.4)	0.690	5.6 (-1.2, 12.5)	0.107
Comorbidity index	2.6 (0.5, 4.7)	0.017	0.4 (-1.7, 2.4)	0.727
Insurance, yes	27.6 (-15.8, 70.9)	0.211	15.5 (-21.9, 52.9)	0.414
History of glaucoma filtering surgery, yes	10.4 (0.0, 20.8)	0.050	3.4 (-7.0, 13.7)	0.523
Visual acuity, per 0.1 LogMAR	6.9 (3.1, 10.8)	0.001	2.9 (-1.1, 7.0)	0.156
Baseline 24-2 MD, per 1 dB worse	2.3 (1.5, 3.1)	< 0.001	2.0 (1.1, 2.9)	< 0.001
Rate of change in 24-2 MD, per 1 dB/year faster loss	13.5 (5.8, 21.3)	0.001	12.5 (4.5, 20.6)	0.003

LogMAR: logarithm of the minimum angle of resolution, MD: mean deviation.

Values are represented as mean (95% confidence interval).

* Statistically significant *P*-values (≤ 0.05) are shown in bold.

Table 3.

Results of the Univariable and Multivariable Regression Models for the Association between Baseline and Initial Rates of Change in 24-2 Visual Field Mean Deviation of the Worse Eye and National Eye Institute Visual Function Questionnaire-25 Score (n = 167)

Characteristic	Univariable Model		Multivariable Model	
	Coefficient	<i>P</i> -value*	Coefficient	<i>P</i> -value*
Age, per decade older	2.1 (-1.4, 5.6)	0.236	0.7 (-3.0, 4.3)	0.721
Gender, female	8.5 (1.9, 15.1)	0.012	10.1 (3.0, 17.2)	0.006
Race, African American	3.7 (-3.0, 10.4)	0.275	0.2 (-6.5, 7.0)	0.949
Education level, at least high school degree	-11.2 (-29.2, 6.8)	0.221	2.9 (-15.0, 20.8)	0.751
Income, <\$25000	17.4 (6.4, 28.4)	0.002	17.3 (6.6, 27.9)	0.002
Marital status, married	-1.4 (-8.1, 5.4)	0.690	5.9 (-1.1, 12.9)	0.100
Comorbidity index	2.6 (0.5, 4.7)	0.017	1.0 (-1.2, 3.1)	0.373
Insurance, yes	27.6 (-15.8, 70.9)	0.211	16.8 (-21.5, 55.1)	0.388
History of glaucoma filtering surgery, yes	9.3 (1.2, 17.3)	0.024	0.6 (-8.2, 9.5)	0.890
Visual acuity, per 0.1 LogMAR	4.3 (2.1, 6.5)	< 0.001	2.3 (-0.1, 4.7)	0.063
Baseline 24-2 MD, per 1 dB worse	1.2 (0.7, 1.7)	< 0.001	1.1 (0.6, 1.7)	< 0.001
Rate of change in 24-2 MD, per 1 dB/year faster loss	2.8 (-2.0, 7.7)	0.251	3.7 (-0.9, 8.3)	0.109

LogMAR: logarithm of the minimum angle of resolution, MD: mean deviation.

Values are represented as mean (95% confidence interval).

* Statistically significant *P*-values (≤ 0.05) are shown in bold.

Table 4.

Results of the Linear Regression Models for the Prediction of the NEI VFQ-25 Scores Based on Baseline and Initial Rates of Change of 24-2 MD in the Better and the Worse Eyes (n = 167)

Eye	Variable	Coefficient (95% CI)	<i>P</i> -value*	R ²	BIC
Better	Baseline MD, per 1 dB worse	2.25 (1.44, 3.07)	< 0.001	0.21	1478.82
	Initial rate of change of MD, per 1 dB/year faster loss	12.88 (5.73, 20.03)	< 0.001		
Worse	Baseline MD, per 1 dB worse	1.24 (0.78, 1.70)	< 0.001	0.15	1490.56
	Initial rate of change of MD, per 1 dB/year faster loss	3.93 (-0.58, 8.43)	0.087		

NEI: national eye institute, VFQ-25: 25-item visual function questionnaire, VF: visual field, CI: confidence interval, BIC: Bayesian information criterion.

* Statistically significant *P*-values (< 0.05) are shown in bold.

Table 5.

Results of the Linear Regression Models for the Prediction of the NEI VFQ-25 Scores Based on Baseline and Initial Rates of Change of the Peripheral and Central Test Locations of the Binocular 24-2 Mean Sensitivity (n = 167)

Test location	Variable	Coefficient (95% CI)	P-value*	R ²	BIC
Peripheral	Baseline, per 1 dB worse	3.58 (2.33, 4.82)	< 0.001	0.20	1480.92
	Rate of change, per 1 dB/year faster loss	14.39 (4.93, 23.85)	0.003		
Central	Baseline, per 1 dB worse	4.73 (3.33, 6.13)	< 0.001	0.25	1470.18
	Rate of change, per 1 dB/year faster loss	19.50 (9.18, 29.81)	< 0.001		

NEI: national eye institute, VFQ-25: 25-item visual function questionnaire, VF: visual field, CI: confidence interval, BIC: Bayesian information criterion.

* Statistically significant P-values (< 0.05) are shown in bold.