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SYSTEMATIC REVIEW AND META-ANALYSIS

Location of visual field defects and their impact on vision-related quality of life in glaucoma: A systematic review

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ABSTRACT

Background: Regional patterns of visual field (VF) loss may affect vision-related quality of life (QoL) differently in people with glaucoma; yet evidence across studies remains inconsistent.

Objectives: To identify and evaluate studies comparing vision-related QoL, measured by the National Eye Institute Visual Function Questionnaire (NEI-VFQ-25), with specific regions of VF loss in glaucoma.

Data Sources: MEDLINE, EMBASE, CINAHL, PsycINFO, and AMED were systematically searched from inception to April 2025.

Study Eligibility Criteria: Eligible studies included adults with glaucoma that examined regional VF loss (e.g., central vs. peripheral, hemifield, or cluster analyses) and reported NEI-VFQ-25 outcomes. Studies using only global VF indices were excluded.

Study Appraisal and Synthesis Methods: Two reviewers independently screened studies, extracted data, and assessed methodological quality using the Joanna Briggs Institute tools. Due to heterogeneity in VF metrics and NEI-VFQ-25 scoring approaches, the findings were synthesized narratively.

Results: Nine studies (n = 2626 participants) met the inclusion criteria. Most cohorts were relatively young (mean age mid-60s) with mild–moderate glaucoma; only two included participants with advanced loss. Despite methodological variation, a consistent pattern emerged: central and inferior VF loss were most strongly associated with poorer QoL, whereas superior and peripheral loss showed weaker or domain-specific effects. Associations were generally stronger when using better-eye or integrated VF measures.

Limitations: The evidence base is limited by few studies, small sample sizes, predominance of mild disease, and variability in both VF and NEI-VFQ-25 methodologies.

Conclusions and Implications of Key Findings: Central and inferior VF loss appear most closely linked to reduced QoL; however, conclusions are constrained by the limited number and methodological heterogeneity of available studies. Larger, standardized investigations across disease stages are needed to clarify these relationships and guide patient-centered care.

Trial Registration: PROSPERO CRD420251169334.

INTRODUCTION

Glaucoma is a progressive optic neuropathy characterized by the gradual loss of retinal ganglion cells, which in turn leads to marked visual field (VF) defects.[1] These VF losses are usually measured and monitored via standard automated perimetry (SAP) instruments, such as the Humphrey Field Analyzer (HFA). As VF loss progresses, the glaucomatous damage reduces individual's vison-related quality of life (QoL) in modalities such as mobility, reading, and driving,[2] with faster loss equating to higher likelihood of poorer self-reported QoL.[3,4] Patient-reported outcome measures (PROMs) are therefore essential, as they rely on self-reported questionnaires to capture the functional impact of glaucoma on everyday life.[5]

The 25-item National Eye Institute Visual Function Questionnaire (NEI-VFQ-25) is a widely used PROM designed to specifically assess vision-related QoL.[6,7] It has been extensively applied in glaucoma research, including large clinical trials. For example, the Treatment of Advanced Glaucoma Study (TAGS)[8] used the NEI-VFQ-25 as its primary outcome measure, wheras the Ocular Hypertension Treatment Study (OHTS) incorporated it to characterize impact among individuals at risk of glaucoma progression.[9] The NEI-VFQ-25 summarizes vision-related experience across multiple domains, including near and distance vision activities, ocular pain, social function, role function, mental health, dependency, driving difficulties, color vision, and peripheral vision, as well as a composite score encompassing all of those domains.[6,7] Scores for the PROM range from 0 to 100, with higher scores indicating better vision-related QoL. Early work in 1997 demonstrated a steady linear decline between VF loss and vision-related QoL using the NEI-VFQ-25 in 147 people with glaucoma, indicating that preventing early VF loss may be important for maintaining patient QoL.[10]

Greater overall VF loss is associated with poorer vision-related QoL,[10–12] yet the *location* of damage is likely to shape how patients experience visual difficulties. Retinal ganglion cells are densely concentrated centrally,[13] and glaucomatous damage follows nerve fiber bundle patterns that produce region-specific deficits.[14] It is plausible that certain VF regions contribute more critically to daily visual function than others. Empirical data studies support this proposition. For example, Black et al. (2011) demonstrated that inferior hemifield loss was associated with worse functional performance (e.g., weaker lower limb strength, lower self-reported physical activity), impaired postural stability, and increased risk of falls, whereas superior loss showed less functional impact.[15,16] However, behavioral adaptations may partly mitigate these effects, as individuals with glaucoma can adopt compensatory eye movements such as increasing saccades toward areas of field loss which may help maintain performance in everyday tasks.[17–21] Yet, two individuals with similar summary measures of VF loss (e.g., mean deviation [MD]) may function very differently if one has central loss whereas another has inferior or peripheral loss, particularly depending on whether or not the pattern of damage between the two eyes leads to binocular vision loss.[22] Understanding these location-specific effects is clinically relevant for patient counseling, monitoring strategies, and treatment prioritization.

Significance

The evidence for regional patterns of VF loss and their association with vision-related QoL, as measured by the NEI-VFQ-25, remains limited due to the small number of heterogenous studies, small sample sizes, and predominance of mild disease. There is a clear need for larger, standardized studies to optimize patient care.

The aim of this review is to: (1) identify existing literature comparing QoL via NEI-VFQ and VF assessments in individuals with glaucoma; (2) assess the volume and quality of available studies; and (3) assess findings regarding locations of defects and their relation to self-reported vision-related QoL.

METHODS

Eligibility criteria for considering studies for this systematic review

To be eligible for inclusion, studies had to: (1) be published in the English language; (2) include participants with any type of stage of glaucoma (though a mixture of glaucoma and hypertensive patients was accepted); (3) report region-specific analyses of the VF (i.e., not just global indices such as MD, or Visual Field Index [VFI], but also hemifield-based, central versus peripheral, or cluster/grouped point analyses, as well as studies reporting raw pointwise data); and (4) feature a version of the NEI-VFQ PROM (either the standard 25-item form or a validated subtype). Studies were excluded if they were review articles, letters to the editor, published protocols or conference abstracts.

Search methods for identifying studies

This systematic review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. The review protocol was prospectively registered in the International Prospective Register of Systematic Reviews (PROSPERO; registration number CRD420251169334). The following databases were searched for studies from inception to the present: CINAHL, MEDLINE, PsycINFO (via EBSCO) and

EMBASE and AMED (via OVID). An indicative list of search terms and the search query used is provided in the search strategy document (see Appendix 1). The reference lists of the included literature were examined as a further source of relevant studies. Covidence software[23] (Veritas Health Innovation, https://www.covidence.org) was used for extraction, organization and screening of the literature.

Study selection

Two authors (B.E.H. and D.P.C.) independently assessed for eligibility for inclusion through screening titles and abstracts. The same two authors then independently read the full texts of potentially eligible studies; any disagreements about inclusion were resolved through discussion and then arbitration by a third author (S.G.). The reference lists of all included studies were also hand-searched to identify any additional relevant articles.

Data collection and risk of bias assessment

Two authors (B.E.H. and D.P.C.) independently evaluated the quality of the included studies. The Joanna Briggs Institute critical appraisal tool[24] (JBI; Joanna Briggs Institute, https://joannabriggs.org) was used to assess both cohort and cross-sectional design types. This tool is recommended by the UK National Institute for Health and Care Excellence[25] (NICE; National Institute for Health and Care Excellence, https://www.nice.org.uk/) guidelines.

Data synthesis and analysis

Study characteristics were extracted into data synthesis s (Tables S2 and S3, and Table 1). A meta-analysis was not conducted due to considerable heterogeneity in study designs, VF reporting methods (e.g., hemifield-based, central vs. peripheral, or cluster/grouped point analyses), glaucoma types, and approaches to NEI-VFQ-25 scoring (raw vs. Rasch calibration). Data were synthesized narratively according to: (1) the VF regions analyzed; (2) the NEI-VFQ-25 subscales and composite scores assessed; and (3) the statistical methods and covariates employed. Key methodological differences such as inclusion criteria, use of covariate adjustment, and analytical approach were also summarized. This review is based solely on previously published studies and does not involve any research with human participants or animals conducted by the authors.

RESULTS

Search results

The search of bibliographic databases performed on 9 April 2025 identified 433 publications; 164 were identified

TABLE 1 Summary of modeling approaches and covariate treatment across studies.

Study	Modeling approach	Covariates considered in models	Related results
Moghimi et al. (2023) [26]	Linear regression models	Gender, race, education, income, marital status, health insurance, comorbidity index. Baseline VF severity and rate of VF change analyzed separately and jointly.	Better-eye baseline severity and rate of decline were independent predictors of NEI-VFQ-25 score. Income and female sex also associated with worse QoL.
McKean-Cowdin et al. (2007) [27]	ANCOVA and linear regression models	Age, gender, education, employment, income, acculturation, insurance (health and vision), comorbidity count, VA, awareness of glaucoma diagnosis	All covariates remained in adjusted models (as per design). Fully adjusted models still showed large effects for central VF loss on composite and subscales
Cheng et al. (2015) [28]	Multivariable linear regression models	Age, sex, education, income and medication burden. Variables with $p < 0.10$ in univariate + habitual binocular VA and IVF MD forced into models.	Retained: Age (greater age associated with lower QoL), higher education (better QoL), better habitual binocular VA, coronary artery disease, glaucoma medication frequency, IVF MD.
Chun et al. (2019) [29]	Hierarchical multivariable linear regression models	Age, sex, education, income, cohabitation, systemic comorbidity index, habitual VA, number of glaucoma meds; variables with $p < 0.20$ in univariate included.	Models were adjusted for these factors; the paper does not single out specific covariates as consistently significant.
Lee et al. (2021) [30]	Univariate and multivariable linear regression models	Age, binocular IVF measures, VA, number of medications (entered if $p < 0.20$ in screening)	After adjustment, binocular inferior IVF and binocular whole IVF were the strongest independent predictors
van Gestel et al. (2010) [31]	Multiple linear regression models	Age, sex, VA (better and worse eye), side effects of glaucoma medication, prior laser or surgical treatment	VA and medication side effects were significant contributors to NEI-VFQ-25 scores.

Abbreviations: IVF; integrated visual field; MD, mean deviation; NEI-VFQ-25, National Eye Institute Visual Function Questionnaire-25; QoL, quality of life; VA, visual acuity; VF, visual field.

as duplicates, leaving 269 for abstract review. Of these, $n = 248$ (92%) were excluded during abstract screening on the basis of being irrelevancy or failure to meet the inclusion criteria. Twenty-one were included in the full text assessment, of which eight papers were deemed appropriate for the final review process. During citation searching of included studies, one additional relevant study was identified and included, resulting in nine studies in the final review (Figure 1). The two reviewers agreed regarding inclusion decisions and no arbitration was required.

Quality appraisal

The nine included studies[26–34] were predominantly cross-sectional by design. Two studies had longitudinal designs: Abe et al. (2015) had a prospective cohort design and Moghimi et al. (2023) had a retrospective cohort design. Methodological quality was appraised using the JBI Critical Appraisal Checklist for Analytical Cross-Sectional Studies and Cohort Studies. The grading of all papers is presented in Table S1.

All studies used validated measures such as the HFA and the NEI-VFQ-25. The most common source of potential bias was **c**onfounding bias, as a few cross-sectional studies[32,34] did not adjust for key covariates such as visual acuity (VA), age, glaucoma severity, or other socio-demographic factors that may impact the relationship between VF loss and vision-related QoL. Overall, no studies were removed from this review based on bias assessment, though results should be interpreted cautiously where confounding bias may have influenced findings.

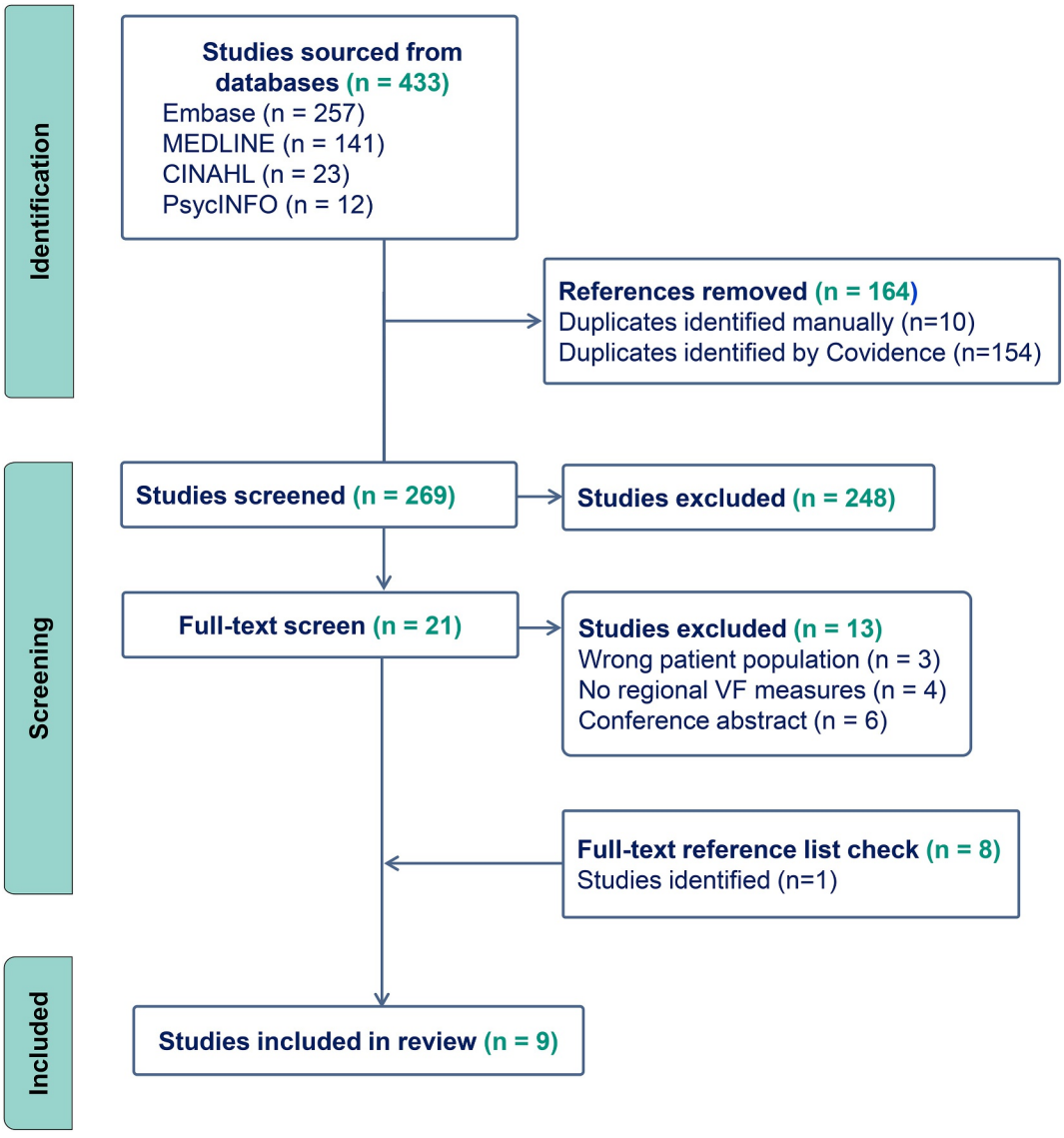

FIGURE 1 PRISMA flowchart.

Overview of included studies

Nine studies met the inclusion criteria of this review. They featured data from a total of $n = 2626$ people with varying types of glaucoma and ocular hypertension (OHT). Most studies were modest in size (median sample size was 186 participants [range 138–826]). Chun et al. (2019) featured a notably larger sample size of 826 participants, whereas van Gestel et al. (2010) featured 531 participants (note: $n = 189$ [36%] had OHT rather than glaucoma). Four studies were conducted in the USA,[26,27,33,34] two in Korea,[29,30] one in Japan,[32] one in the Netherlands[31] and one in Taiwan.[28] All studies utilized the NEI-VFQ-25 questionnaire, with four using translated versions: two in Korean, one in Japanese, and one in Chinese (Taiwan version).

Most participants had open-angle glaucoma (OAG), most commonly primary OAG (POAG; $n = 1519$) or normal-tension glaucoma (NTG; $n = 186$). Smaller numbers of pseudoexfoliation glaucoma ($n = 7$) and angle-closure glaucoma ($n = 6$) were also reported.[34] Several studies included mixed cohorts (e.g., POAG and NTG[30,32,34] and POAG and OHT[31]), whereas one study reported both glaucoma-suspect and confirmed glaucoma eyes.[26] In the longitudinal study by Moghimi et al. (2023), glaucoma-suspect eyes were followed for almost a decade to determine whether rates of VF progression predicted later patient-reported QoL, thereby capturing the transition from minimal or no loss to established disease. van Gestel et al. (2010) included OHT participants to evaluate QoL across the full spectrum of glaucoma severity; these individuals were analyzed within the main cohort rather than as separate controls. However, repeat analyses restricted to POAG patients yielded unchanged conclusions. Notably outside of this review, Nishida et al. (2022) found reduced QoL even in POAG patients who did not yet have repeatable VF defects.[35]

Participant demographics were broadly similar across studies. As detailed in Table S2, mean ages ranged from approximately 58–73 years, with most cohorts having a mean age in the mid-60s. Across studies where sex was reported, approximately 46% of participants were female. Ethnicity varied by study location: US-based cohorts included White, African American and Latino participants, whereas studies conducted in Korea, Japan and Taiwan predominantly included East Asian participants. van Gestel et al. (2010) did not report ethnicity.

Visual field loss varied across studies; although most cohorts only included individuals with mild to moderate glaucomatous damage (moderate loss being ~−10 dB). Where reported, MD in the better eye ranged from −1.6 to −8.5 dB, whereas mean MD in the worse eye ranged from −3.8 to −14.5 dB across studies, indicating mild and moderate VF impairment, respectively. Moghimi et al. (2023) distinguished newly diagnosed from previously diagnosed glaucoma, with newly diagnosed participants demonstrating milder loss (better/worse eye MD −4.3/−8.7 dB) compared to those with established disease (−7.6/−13.1 dB).[26] Based on the better eye MD, Sawada et al. and the previously diagnosed subgroup in McKean-Cowdin et al. represented the cohorts with more advanced VF loss (−8.5 dB and −7.6 dB, respectively),[27,32] whereas the remaining studies predominantly included individuals with mild-to-moderate disease[26,28–30,33,34] and van Gestel et al. included individuals with OHT.[31]

Despite a shared use of the NEI-VFQ-25 to assess self-reported visual function and the HFA to assess VF loss, the studies demonstrated differences in VF methodology, analytical approach, and sample characteristics, making direct comparisons difficult. Key differences included variation in analysis methods of VF test results (monocular vs. integrated VF [IVF] approaches), glaucoma type (and their severity level), differences in VF region definitions (hemifield-based, central vs. peripheral, or cluster/grouped point analyses) and NEI-VFQ-25 scoring methods (calibrated vs. raw). Here, central is defined as the points located in the region encompassing approximately the central 10° of the VF. Adjustment for covariates such as VA, age, education level, comorbidities and income was inconsistent across studies.

A narrative synthesis of findings from the nine included studies follows, focusing on how regional VF impairment (central, inferior, superior, or peripheral) relates to self-reported vision-related QoL. Study details are provided in Tables S2 and S3, and Table 1.

Patterns of association between VF regions and QoL outcomes

Studies defined VF location using hemifields, quadrants, or clusters. For comparability, we synthesized results by four regions (central, inferior, superior, and peripheral). Where cluster-based analyses were used, the authors assigned each cluster to its predominant anatomical region (e.g., paracentral clusters were allocated to central). For a summary of the main associations between VF regions and NEI-VFQ-25 subscales covered by the eight studies, see Table S3. For consistency and ease of comparison, r (correlation coefficients) have been transformed to R^2 (coefficient of determination) throughout.

Central visual field

Across the studies, central VF loss emerged as the most consistent and strongest predictor of reduced vision-related QoL. When assessed in the better eye,[32,34] reduced sensitivity in central and paracentral clusters was significantly associated with lower NEI-VFQ-25 composite scores and subscales relating to distance vision, driving,

mobility, dependency, and social functioning, with moderate correlation strengths.

Studies using binocular metrics such as Moghimi et al. (2023) demonstrated that central IVF sensitivity explained more variance in vision-related QoL than peripheral regions (central $R^2 = 0.25$ vs. peripheral $R^2 = 0.20$), and Abe et al. (2015) showed that progressive decline in the central inferior field predicted decline in vision-related QoL longitudinally ($R^2 = 0.35$). Chun et al. (2019) found that the superior central region was the most influential field location assessed, associated with worse composite score and subscales related to near activities, social functioning, and role difficulty ($R^2 \approx 0.14$–0.18).

Inferior visual field

Inferior VF damage was also associated with vision-related QoL, more so than superior, particularly for subscales focused on maintaining independence and good mental health. Sawada et al. (2014) reported that the lower paracentral and lower peripheral regions in the better eye were significantly associated with declines in composite scores and most subscales, including near and distance vision, role function mental health and driving ($R^2 \approx 0.16$–0.26). These were among the strongest effects reported in this review. The lower central cluster of the better eye was also found to be correlated with the composite score, mental health, and driving subscales ($R^2 \approx 0.16$–0.20).[32]

Evidence from longitudinal analyses reinforce this. Abe et al. (2015) showed that progressive loss in the central inferior IVF region was the strongest predictor of a decline in vision-related QoL over time (central inferior $R^2 = 0.35$, peripheral inferior $R^2 = 0.30$). Cheng et al. (2015) further demonstrated that inferior hemifield sensitivity was associated with poorer general vision, role difficulties, and peripheral vision subscales ($R^2 \approx 0.12$–0.21) whereas Chun et al. (2019) reported that the region correlated with distance vision, mental health, and dependency domains ($R^2 = 0.12$–21). van Gestel et al. (2010) also found that inferior binocular VF loss had approximately double the impact on composite scores compared with superior loss (0.70 vs. 0.35 units decline per 1 dB decrease in sensitivity), indicating a stronger functional consequence of inferior field deficits.

Superior visual field

Associations between superior VF loss and QoL appeared to be more domain specific. Sawada et al. (2014) reported that the upper temporal cluster of the better eye was strongly correlated with the driving domain ($R^2 = 0.26$). Cheng et al. (2015) found superior hemifield loss associated with difficulty in near activities (e.g., reading) with $R^2 \approx 0.30$, highlighting the superior field's role in foveal guidance and sustained fixation. Chun et al. (2019) similarly identified the superior central IVF region as being associated with worse near activity, social functioning, and role difficulty subscales ($R^2 \approx 0.14$–0.18).

Peripheral visual field

The effect of peripheral VF loss on vision-related-QoL was variable. Although Moghimi et al. (2023) found peripheral region correlated with the composite score ($R^2 = 0.20$), they reported that the central region had a greater association ($R^2 = 0.25$). McKean-Cowdin et al. (2007) showed that isolated peripheral loss produced modest reductions (effect size for composite score ≈ 0.75), but combined central and peripheral involvement resulted in much larger effects (subscale effect size increased up to 1.74). Here, "effect size" is the standardized mean difference that is, the adjusted NEI-VFQ-25 score difference between groups, divided by the no-loss group's standard deviation. Sun et al. (2016) and Sawada et al. (2014) similarly noted that peripheral field involvement increased functional impact when co-occurring with inferior or paracentral damage, particularly affecting driving and role performance.

Better versus worse eye and binocular considerations

Across studies, the VF of the better eye were more strongly correlated with NEI-VFQ-25 scores than the worse eye alone. Sun et al. (2014) and Sawada et al. (2016) reported stronger associations between the better eye clusters and QoL subscales. Moghimi et al. (2023) showed that baseline and rate of decline in the better eye MD were more predictive of NEI-VFQ-25 scores than equivalent parameters from the worse eye. However, when examining regional effects, this study used IVF.[36] Other studies using IVF approaches[28–30,33] demonstrated clear and consistent regional relationships between VF loss and NEI-VFQ-25 outcomes. For example, IVF-based central and inferior regions explained a greater proportion of variation in QoL scores (e.g., inferior central IVF $R^2 = 0.35$ in Abe et al.), suggesting measures reflecting binocular vision may better capture functional impact than monocular indices.

Methodological heterogeneity

Methodological heterogeneity limited direct comparison across studies. Definitions of VF regions varied substantially, ranging from cluster-based classifications of 24-2 test locations[34] and 30-2 test locations,[32] to hemifield analyses comparing superior versus inferior IVF sensitivity,[28,30,31]

central versus peripheral[26,27] and four quadrant divisions.[29,33]

Scoring approaches for the NEI-VFQ-25 also differed, with some studies using Rasch-calibrated data[26,29,33] whereas the others used raw scores. Different Rasch calibrations were applied: two analyzed items within grouped rating-scale structures,[26,33] whereas Chun et al. (2019) used partial credit models allowing item-specific thresholds.[29] In two studies, VFQ-25 items related to dependency, mental health, role limitations, and ocular pain were excluded during Rasch calibration due to multidimensionality.[26,33] Cheng et al. (2015) applied a rank-based normalization procedure to NEI-VFQ-25 scores (PROC RANK), producing transformed values rather than raw or Rasch-calibrated scores. McKean-Cowdin et al. (2007) analyzed log-transformed raw NEI-VFQ-25 scores to address ceiling effects, rather than Rasch calibration or untransformed scoring.

Degree of covariate adjustment was inconsistent. Sun et al. (2016) and Sawada et al. (2014) reported only unadjusted associations. In contrast, six studies[26–31] incorporated covariates into regression models when examining the relationship between VF region and vision-related QoL (see Table 1). These studies adjusted for sociodemographic, clinical and, in some cases, socioeconomic and systemic comorbidity variables when examining the relationship between regional VF damage and vision-related QoL. Although Chun et al. (2019) employed a hierarchical regression framework, providing a slightly more sophisticated assessment of incremental contributions, all six studies in Table 1 are fundamentally more informative than Sun et al. or Sawada et al. because they accounted for potential confounding factors. Abe et al. (2015) used a longitudinal joint mixed-effects model to assess change in NEI-VFQ-25 scores in relation to progressive binocular sensitivity loss over time, rather than cross-sectional regional comparisons. As the focus was on rate of decline rather than adjustment for demographic or socioeconomic confounding, the study was not directly comparable to the covariate-based analyses featured in Table 1. Overall, the strength of association between regional VF loss and NEI-VFQ-25 scores was influenced by the extent of covariate adjustment. Studies controlling for VA and socioeconomic factors showed some impact, but central and inferior VF loss consistently remained independently associated with poorer QoL. Sex or gender (as reported by individual studies) was included in several multivariable models as an adjustment variable rather than a primary factor of interest. For example, Moghimi et al. (2023) identified female gender as associated with worse overall NEI-VFQ-25 scores, whereas Chun et al. (2019) retained sex within hierarchical models (e.g., associations with driving-related scores), although none of these studies evaluated whether sex or gender identity modified the relationship between VF defect location and QoL.

DISCUSSION

This review identified only nine studies that examined the relationship between regional VF defects and vision-related QoL, as measured by the NEI-VFQ-25 in people with glaucoma. Most of the included studies were relatively small (≤236 participants, with an exception at 826 participants[29] and 531 participants [with 36% having OHT][31]). Across the included studies, cohorts were relatively young (mid-60s) and predominantly experiencing mild-to-moderate VF loss, particularly in the better-seeing eye. Correlations were generally moderate ($R^2 \approx 0.20$), even in studies that adjusted for major covariates, which is unsurprising given the expected test–retest variability both in subjective measures of QoL and in VF sensitivities. Despite this variability, together with the predominance of participants with early or moderate disease, the similarities in conclusions supports a relationship between regional VF loss and vision-related QoL decline.

Across the studies, central[26,29,32–34] and inferior[28–33] VF loss was most consistently associated with poorer QoL, as measured by the NEI-VFQ-25. Superior VF loss affected some subscales (most notably near activities and driving)[28,29,32] but had less effect on the composite score compared to other regions. When greater weight is given to studies specifically designed to evaluate regional VF defects in relation to NEI-VFQ-25 outcomes—which considered hemifield distinctions beyond central versus peripheral and adjusted for potential confounders[28,29,33]. These studies also typically identified inferior and central field damage as the regions most strongly associated with reduced QoL.

Studies outside this review also reinforce the disproportionate role of central and inferior VF regions in daily visual functioning. For example, Black et al. (2011) assessed participants' functional status via a combination of physical tasks and self-report and reported that inferior hemifield loss predicted poorer functional status and postural stability, whereas superior loss did not.[16] In addition, Black et al. reported, loss in this region was also associated with higher rate of falls and falls with injury.[15] Sumi et al. (2003) used their own disability index and similarly found that inferior paracentral sensitivity was the strongest independent predictor of patient-reported disability after adjusting for VA, whereas superior and peripheral measures did not retain significance.[37] Murata et al. (2013), using binocular IVF maps and machine learning, showed that task performance and overall vision-related QoL were most strongly influenced by points along the central horizontal meridian and inferior paracentral/mid-peripheral regions, especially for mobility-related activities such as walking,[38] consistent with the findings of Black et al. Blumberg et al. (2017) demonstrated that 10-2 central field sensitivity showed a stronger association with NEI-VFQ-25 scores than 24-2

testing, explaining functional difficulties in patients whose 24-2 fields appeared relatively preserved.[39]

Recent simulation work in normally sighted individuals further support these findings.[40–42] For example, Jones et al. used virtual/augmented realty to simulate VF loss and found that inferior defects caused substantially worse performance and perceived difficulty than superior defects—nearly equivalent to the difference between having superior loss and no loss at all—highlighting the functional importance of the inferior field.[42] Yet, due to heterogeneity between studies and the small number of studies, it is not possible from the literature to determine the likely impact of more precisely localized defects; for example, whether a defect that spans 5–10° eccentricity in the inferior field has the same impact as a defect spanning 10–20° eccentricity in the same hemifield.

Intuitively, the importance of central VF loss would be expected. The macular region, with its much higher density of photoreceptors and retinal ganglion cells,[13] is used for many activities of daily living, including any that require observation of fine details, such as reading. However, VF loss outside of the central 5° (the region tested by the central 4 locations of the 24-2 VF) still has a substantial impact on QoL. Mid-peripheral vision is highly important for many activities, such as balance, obstacle avoidance, and driving.[32] This is particularly true in the inferior field, which is essential for avoiding tripping hazards; implying that inferior loss would be expected to have a greater impact on mobility, and patients' confidence while mobile, than equal severity of loss at the same eccentricity in the superior field. The inferior left region of the VF is particularly important for reading in most languages, since it is used when moving to the next line of text.[17] The importance of the mid-peripheral VF is also amplified in low light conditions due to the spatial distributions of rod and cone photoreceptors. Thus, the impacts of glaucoma and other ocular diseases on QoL are diluted in studies that rely solely on global indices summarizing the severity of loss, and by studies such as those included here that only divided the VF into central versus peripheral without regard to hemifield.[26,27]

The included studies derived from four different countries (USA, Netherlands, Japan, Korea and Taiwan), and cultural differences cannot be discounted. Reading direction varies across languages (horizontal or vertical in East Asia vs. left-to-right in the USA and Europe). Driving side also differs by country, affecting the relative importance of the left and right VF. Hazard exposure may further vary between urban and rural environments. Additionally, subtle differences in translated survey versions cannot be ruled out.

Despite the importance of the topic, the number of papers identified as meeting the inclusion criteria was very small ($n = 9$). Only English language papers were included in the review, possibly resulting in omission of relevant studies. Conference abstracts were also excluded; so, emerging data may have been missed. Only published peer-reviewed studies were included, and there is always the possibility of publication bias, whereby nonsignificant associations are less likely to be reported in journals. It was not possible to conduct a meta-analysis of the included studies, due to substantial methodological heterogeneity. Additionally, the cross-sectional nature of most studies precludes any inference about causality.

Some studies used the raw scores from the questionnaire, whereas others used a Rasch calibration approach,[26,29,33] a form of Item Response Theory, to transform ordinal responses into interval-level measurements. This improves scale linearity, reduces measurement noise and may produce more statistically valid conclusions. Yet, the calibration is specific to the particular dataset used and different Rasch calibrations can be applied, presenting a further barrier to comparisons between studies. Psychometric analyses have shown that the NEI-VFQ-25 may be multidimensional in low-vision groups, reflecting constructs of both visual function and emotional impact.[43] In glaucoma populations, items related to dependency, mental health, role limitations, and ocular pain have been subsequently excluded when calculating Rasch-calibrated person measures.[4,26,33] These methodological choices highlight the fact that composite scores may obscure domain-specific associations between VF loss and patient-reported function; yet this is not agreed upon.[44] Nevertheless, Rasch calibration can affect what aspects of vision-related QoL are captured, contributing to heterogeneity in reported associations across studies.

Although the NEI-VFQ-25 provides valuable insight into patient-reported vision-related QoL, it is not glaucoma-specific and may not fully capture outcomes most relevant to this population, such as specific functional deficits (peripheral vision or glare) or mobility limitations.[45] Glaucoma-specific PROMs, which include the Glaucoma Quality of Life-15 Questionnaire[45] or the Glaucoma Utility Index,[46] may address these limitations and are utilized by the research community,[47,48] though their use remains less widespread when compared to the NEI-VFQ-25. Overall, both the potential multidimensional nature of the NEI-VFQ-25 and variability in Rasch calibration approaches should be considered when interpreting evidence linking VF defect location to QoL in glaucoma.

There was also inconsistency over whether to use the better eye, or an integrated binocular VF. Studies that compared better and worse eye, found that the better eye had greater influence over vision-related QoL,[27,31,32,34] likely because the worse eye's contribution is lower in binocular activities. Yet, impairment of the worse eye does appear to negatively impact QoL in certain domains.[32] This highlights that binocular processing is complex, as in some cases it can improve functional vision, whereas in others, binocular inhibition can occur when defects do not overlap, thus reducing visual performance.[22] In many subjects using an IVF is essentially equivalent to using the

better eye, but they can differ substantially. In the worst-case scenario, a person could have an absolute inferior hemifield defect in one eye, and an absolute superior hemifield defect in the fellow eye, giving moderate/severe monocular loss in both eyes but a near normal IVF. Taken together, these findings highlight that both monocular VFs of each eye and the IVF should ideally be examined when evaluating the impact of VF loss on vision-related QoL.

The inability to perform meta-analyses means that further studies are needed to generate more definitive conclusions about the effect of localized loss on QoL, addressing these methodological gaps. The potential benefits of using a Rasch calibration versus raw scores need further exploration in people with glaucoma before a recommendation can be made, but currently it appears that including both has its merits. For example, a recent study comparing VA to Rasch-calibrated and nonRasch-calibrated NEI-VFQ-25 scores in people with proliferative diabetic retinopathy[44] found minimal differences between the combined Rasch calibration and the original composite score (R^2 = 0.17 and 0.15, respectively). Thus, Rasch calibration may improve measurement precision and scale linearity, but the raw composite score may still give meaningful insights into vision-related QoL, and analyses based on the raw scores should not be disregarded. A similar study in people with glaucoma should be conducted.

A standardized VF localization framework should be used that allows discrimination between the regions that would be expected to impact QoL in different ways. At a minimum separating the impacts on QoL of paracentral defects from mid-peripheral and peripheral defects, further split into superior versus inferior, and preferably with the possibility of also splitting left versus right for subscales where that may be important (e.g., driving and reading). Future studies should also incorporate appropriate adjustment for relevant demographic, clinical, and socio-economic covariates such as age, ethnicity, biological sex and gender identity. Due to the high variability associated with any subjective metrics, in particular for NEI-VFQ-25 subscales whose scores are based on only two or three individual questions, and the increase in variability when using regions of the VF instead of global metrics, a very large and diverse dataset would be needed covering a wide range of severities of binocular vision loss.

CONCLUSIONS

Despite these shortcomings of the existing literature, it is still possible to draw several conclusions. The location of VF loss needs to be considered when assessing the likely impact of glaucoma on QoL, not only in research studies but also in clinic. For example, two patients may have the same mean MD but very different patterns of VF loss: one with central or inferior paracentral loss may struggle with reading, mobility, or navigating stairs, whereas another with peripheral superior loss may experience fewer difficulties in these domains. These differences may be considered when making clinical management decisions and when counseling patients about their disease. Future research using large, diverse datasets with standardized VF localization frameworks is needed to better quantify how specific VF regions impact QoL and to guide personalized patient care.

AUTHOR CONTRIBUTIONS

Bethany E. Higgins: Conceptualization; data curation; writing—original draft; writing—review and editing. **David P. Crabb**: Conceptualization; data curation; writing—review and editing; supervision. **Pete R. Jones**: Conceptualization; writing—review and editing. **Stuart K. Gardiner**: Conceptualization; writing—review and editing; supervision.

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CONFLICT OF INTEREST STATEMENT

The authors declare no conflicts of interest.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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APPENDIX 1

1. "non-central visual impairment*" OR "non-central vision loss" OR "peripheral visual impairment*" OR "peripheral vision loss" OR "paracentral visual impairment*" OR "paracentral vision loss" OR "peripheral scotoma*" OR "paracentral scotoma*" OR "glaucoma" OR "retinitis pigmentosa" OR "RP" OR "Optic Neuropath*" OR "Ischemic Optic Neuropath*" OR "Hemianopia" OR "Quadrantanopia"

AND

- "NEI VFQ" OR "NEI-VFQ" OR "NEIVFQ" OR "NEI VFQ-25" OR "NEI-VFQ-25" OR "NEI VFQ 25" OR "NEIVFQ-25" OR "NEI VFQ-39" OR "NEI-VFQ-39" OR "NEI VFQ 39" OR "NEIVFQ-39" OR "NEI VFQ-9" OR "NEI-VFQ-9" OR "NEI VFQ 9" OR "NEIVFQ-9" OR "NEI VFQ-51" OR "NEI-VFQ-51" OR "NEI VFQ 51" OR "NEIVFQ-51" OR "National Eye Institute Visual Function Questionnaire"

AND

2. "visual field*" OR "perimetry" OR "visual field testing" OR "automated perimetry" OR "static perimetry" OR "Humphrey Visual Field" OR "HFA" OR "Goldmann perimetry" OR "Octopus perimetry" OR "SAP" OR "standard automated perimetry"

NOTE: Nonglaucomatous causes of visual field loss (e.g., retinitis pigmentosa, post-stroke hemianopia, optic neuropathies) were intentionally included in the search strategy to ensure sensitivity, but only studies involving glaucoma were ultimately eligible for inclusion in this review.