

Cross sectional study of depression, anxiety and quality of life in glaucoma patients at a tertiary centre in North Kerala

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Purpose: To determine the magnitude and direction of association of anxiety and depression and the quality of life (QoL) in persons with glaucoma. **Methods:** This prospective cross-sectional study in conducted in a tertiary eye center in north Kerala included glaucoma patients and normal subjects aged 40–80 years. The Patient Health Questionnaire-9 (PHQ-9), the Generalized Anxiety Disorder-7 (GAD-7), Glaucoma Quality of Life (GQOL), and glaucoma evaluation were performed for all participants. One-way analysis of variance was used for statistical analysis. **Results:** The study included 148 subjects with glaucoma and 150 subjects without glaucoma. The prevalence of depression (35.81%) and anxiety (25.0%) was significantly higher in glaucoma patients. In a multivariate regression model, PHQ-9 (adjusted OR: 2.39, 95% CI: 1.31–4.38, $P < 0.001$), GAD-7 (adjusted OR: 2.06, 95% CI: 1.01–4.19, $P = 0.01$) and GQOL (coefficient: 6.92, 95% CI: 4.52–9.31, $P < 0.001$) was significantly associated with glaucoma. The GAD-7 score was significantly higher ($P = 0.02$) in PACG compared to POAG in moderate and severe anxiety. ADL scores (one-way ANOVA, $P = 0.001$) and GQOL scores (one-way ANOVA, $P < 0.001$) were significantly associated with vision impairment and blindness. **Conclusion:** Depression and anxiety are common in glaucoma patients, indicating the need for screening protocols using PHQ and GAD scales to identify persons at risk. The lack of ophthalmic risk factors associated with depression and anxiety emphasizes the importance of psychological evaluation and combined management with a psychiatrist in glaucoma management.

Key words: GAD questionnaire, glaucoma and anxiety, glaucoma and depression, mental health in glaucoma, PHQ questionnaire, quality of life in glaucoma

Population-based studies from South India have reported a prevalence of 1.62%–3.51% for primary open-angle glaucoma (POAG) and 0.5%–4.3% for primary angle-closure glaucoma (PACG).^[1–6] There are an estimated 6.48 million with POAG and 2.54 million people with PACG in India. An estimated 4.5 million people worldwide have moderate to severe vision impairment, and 3.2 million people have blindness attributable to glaucoma.^[7] Glaucoma is a leading cause of blindness (5.81%), and approximately 1.5 million people in India have blindness attributable to glaucoma.^[8]

An estimated 10.9%–24.7% of persons with glaucoma may have depression and nearly 13%–30% may have anxiety.^[9–11] The effects of glaucoma on quality of life are reported from several studies from India,^[12,13] but these studies have not explored specifically the possible associations with depression and anxiety. We designed a cross-sectional study to understand the magnitude of depression and anxiety by using previously validated specific instruments in persons with glaucoma in a population of persons seeking care at a tertiary care eye hospital in north Kerala.

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Methods

The study protocol was approved by the institutional ethics committee and adhered to the tenets of the Declaration of Helsinki. Informed consent was obtained from all participants before enrolment in the study. Consecutive study subjects were recruited from the ophthalmology outpatient and glaucoma unit of the study institute after fulfilling the criteria for inclusion. We included subjects with POAG/PACG in the age group of 40–80 years, with confirmed diagnosis of glaucoma, on regular follow-up, and compliant to prescribed medication. Subjects with secondary glaucoma, with decreased vision attributable to causes other than glaucoma, including age-related cataracts with best-corrected visual acuity $<6/60$ in the affected eye, lost to follow-up or not compliant with medications, with high refractive errors, those who did not complete the entire questionnaire, and those who did not provide informed consent for the study were excluded. Consecutive subjects with normal visual acuity and without any ocular comorbidity were selected as a comparison group for the study.

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Each subject enrolled in the study had a comprehensive ophthalmic examination that included uncorrected and best-corrected visual acuity assessments, slit-lamp biomicroscopy assessment of the anterior chamber, gonioscopy assessments of the angle of the anterior chamber, intraocular pressure assessments using a Goldman applanation tonometer, and posterior segment assessments. Subjects with glaucoma had a visual field assessment using an automated Humphrey perimeter and were further classified as mild, moderate, and severe based on the Hodapp–Parrish criteria.^[14]

We used three study instruments that had been translated in the regional language and validated previously for use in this population. The questionnaires included the Patient Health Questionnaire-9 (PHQ-9), the Generalized Anxiety Disorder-7 (GAD-7), The Glaucoma Quality of Life (GQOL), and a general questionnaire that collected information on activities of daily living. The PHQ-9 questionnaire has nine questions to assess depression and is a depression module that scores each of nine DSM-IV criteria as 0 (not at all) to 3 (nearly every day). The severity of depression is graded as 0–4 (none), 5–9 (mild), 10–14 (moderate), 15–19 (moderately severe), and 20–27 (severe).^[15] Previous studies have reported a sensitivity of 88% and a specificity of 88% for major depression based on a PHQ-9 score of ≥ 10 .^[15] The GAD-7 questionnaire that was used to screen for anxiety includes seven questions and calculated scores from 0 to 3 for every response given by the patient.^[16] Scores of 5, 10, and 15 are taken as cut-off points for mild, moderate, and severe anxiety, respectively. The GQOL is a glaucoma-specific questionnaire that is brief, concise, and easy to administer with good validity and reliability.^[17] The GQOL module has 15 vision-related items and the item-level responses for each factor are coded on a five-point scale (1 = no difficulty and 5 = severe difficulty). Participants who do not perform the activity due to non-visual causes are marked as 0. The GQOL items are grouped into four subscales: 1) Central and near vision (two items); 2) Peripheral vision (six items); 3) Dark adaptation and glare (six items); and 4) Outdoor mobility (one item). The total score is derived by summing all item-level response scores. Higher GQOL-15 scores suggest lower QOL. Subscale scores are derived by coding the item-level responses on a numerical interval scale ranging from 0 (no difficulty) to 100 (severe difficulty). GQOL-15 correlates strongly with visual field loss and other psychophysical measures of visual function.

The questionnaires were self-completed by the participants. A counselor guided individuals who needed help in filing the questionnaire without prompting any answers. The questionnaires were administered in the regional language (Malayalam).

The sample size for the study was estimated as 151 cases and 151 controls based on an 80% power, two-sided confidence level of 95, an anticipated prevalence of depression of 10% in the controls, and the ability to detect a least minimum odds ratio of 2.5 and a case-control ratio of 1:1 for an unmatched case-control allocation.

The study data were entered into an anonymized MS Excel spreadsheet and then exported to SPSS V 20.0 for further analysis. Continuous variables were expressed as mean \pm SD and categorical variables were expressed as proportions. A Fishers exact test was used to compare categorical variables

and the students *t*-test and the one-way analysis of variance test (one-way ANOVA) were used to compare continuous variables. A multivariate regression model that included factors found significant in a bivariate model was used to further explore the association of PHQ-9, GAD-7, and GQOL with glaucoma. Associations were expressed as adjusted odds ratio (OR) or regression coefficient and the 95% confidence intervals (95% CI) around the point estimates. $P < 0.05$ was considered statistically significant.

Results

The study included 148 subjects with glaucoma (66 subjects with PACG and 82 subjects with POAG) and 150 subjects without ocular morbidity. The mean \pm SD age of normal subjects (57.00 ± 10.15) was lower than that of subjects with glaucoma (62.47 ± 9.29) in the study ($P < 0.001$). The baseline characteristics of the study population are presented in Table 1.

All the subjects included in the normal group had normal visual acuity. One hundred (67.57%) subjects with glaucoma had a visual acuity better than 6/18 in the better eye, 41 (27.70%) had a visual acuity between 6/18 and 6/60 in the better eye, and 7 (4.73%) subjects had a visual acuity worse than 6/60 in the better eye. Fifty-six (37.84%) of subjects with glaucoma had mild visual field defects in the better eye, 68 (45.95%) subjects had moderate visual field defects in the better eye, and 24 (16.22%) had severe visual field defects in the better eye. The visual acuity did not differ significantly between POAG and PACG ($P = 0.99$). Mild visual field defects were significantly more common in the PACG group (50.0% vs. 28.05%) compared to POAG while severe visual field defects were more common in the POAG group (18.64% vs. 13.64%) compared to PACG ($P = 0.03$).

Table 2 presents the self-reported limitations of respondents to health-related events. Difficulty in driving, watching TV or reading, and hearing disturbances were significantly higher in persons with glaucoma compared to the normal study population. The overall prevalence of depression and anxiety in the study population was 26.17% ($n = 78$) and 18.46% ($n = 55$), respectively. The prevalence of depression (35.81%, $P < 0.001$) and anxiety (25.00%, $P = 0.004$) was significantly higher in persons with glaucoma compared to the normal study population.

Table 3 presents the distribution of PHQ9, GAD7, ADL, and GQOL scores by subjects with glaucoma and normal subjects. PHQ-9 scores, GAD-7 scores, and GQOL scores were significantly higher in persons with glaucoma, although ADL scores were nearly similar between the two groups. Severe depression and anxiety were found in 6.76% and 4.05% of persons with glaucoma in the study population, respectively.

We used a multivariate regression model to further explore the association of PHQ-9, GAD-7, and GQOL with glaucoma. After adjusting for age, sex, education, widowed, currently working, earning status, and diabetes mellitus in a multivariate logistic regression model, PHQ-9 (adjusted odds ratio: 2.39, 95% CI: 1.31–4.38, $P < 0.001$) and GAD-7 (adjusted odds ratio: 2.06, 95% CI: 1.01–4.19, $P = 0.01$) remained significantly associated with glaucoma. GQOL (coefficient: 6.92, 95% CI: 4.52–9.31, $P = < 0.001$) was significantly associated with glaucoma in a multivariate linear regression model.

Table 1: Comparison of clinic-demographic characteristics between persons with glaucoma and the normal controls in the study

	Normal (n=150)	Glaucoma (n=148)	P
Mean Age±SD	57.00±10.15	62.47±9.29	t-test $P<0.001$
Males	75 (50.00%)	81 (54.73%)	Fishers exact $P=0.41$
Females	75 (50.00%)	67 (45.27%)	
Primary School	34 (22.67%)	51 (34.46%)	Fishers exact $P<0.001$
High School	84 (56.00%)	65 (43.92%)	
Pre-degree	0 (0.00%)	18 (12.16%)	
Degree/PG	32 (21.33%)	14 (9.46%)	
Currently working	69 (46.00%)	24 (16.22%)	Fishers exact $P<0.001$
Currently Married	126 (85.14%)	122 (82.43%)	Fishers exact $P=0.53$
Widowed	7 (4.73%)	18 (12.16%)	Fishers exact $P=0.02$
Sufficient monthly earning	116 (77.33%)	69 (46.62%)	Fishers exact $P<0.001$
Self-reported poor health status	4 (2.67%)	10 (6.67%)	Fishers exact $P=0.09$
Hypertension	36 (24.00%)	50 (33.78%)	Fishers exact $P=0.07$
Diabetes Mellitus	29 (19.33%)	56 (37.84%)	Fishers exact $P=0.001$
Heart Attack	10 (6.67%)	13 (8.78%)	Fishers exact $P=0.52$
Heart diseases	2 (1.33%)	7 (4.73%)	Fishers exact $P=0.10$
Thyroid disorders	15 (10.00%)	11 (7.43%)	Fishers exact $P=0.54$
High Cholesterol	5 (3.33%)	22 (14.86%)	Fishers exact $P<0.001$
Stroke	7 (4.67%)	0 (0.00%)	Fishers exact $P=0.01$
Cancer	9 (6.00%)	4 (2.70%)	Fishers exact $P=0.26$
Arthritis	0 (0.00%)	9 (6.08%)	Fishers exact $P=0.0002$
Asthma	1 (0.67%)	12 (8.11%)	Fishers exact $P=0.001$

Table 2: Comparison of self-reported health-related problems between the normal controls and persons with glaucoma in the study

	Normal	Glaucoma	P
Difficulty in driving	22 (15.49%)	80 (54.05%)	Fishers exact $P<0.001$
Difficulty watching TV/Reading	4 (2.84%)	35 (23.65%)	Fishers exact $P<0.001$
Experiences hearing loss	1 (0.67%)	10 (6.76%)	Fishers exact $P=0.005$
Uses hearing aids	15 (10.00%)	45 (30.41%)	Fishers exact $P<0.001$
Feelings of sadness	2 (1.33%)	22 (14.86%)	Fishers exact $P<0.001$
Excess weight loss in last 6 months	13 (8.67%)	14 (9.46%)	Fishers exact $P=0.84$
Difficulty in passing urine	13 (8.67%)	16 (10.81%)	Fishers exact $P=0.56$
Difficulty in passing stools	8 (5.33%)	18 (12.16%)	Fishers exact $P=0.04$
Accidental Falls	7 (4.67%)	14 (9.46%)	Fishers exact $P=0.12$

In Table 4 we compared the PHQ-9, GAD-7, ADL, and GQOL scores by PACG and POAG. PHQ-9, ADL, and GQOL scores did not differ significantly between POAG and PACG, but moderate and severe anxiety on the GAD-7 score was significantly higher ($P = 0.02$) in PACG compared to POAG. PHQ-9 scores ($P = 0.69$) and GAD-7 scores ($P = 0.42$) were not associated with visual acuity; however, ADL scores (one-way ANOVA, $P = 0.001$) and GQOL scores (one-way ANOVA, $P < 0.001$) were significantly associated with vision impairment and blindness. PHQ-9 scores ($P = 0.26$), GAD-7 scores ($P = 0.64$), ADL scores (one-way ANOVA, $P = 0.60$) and GQOL scores (one-way ANOVA, $P = 0.11$) were not associated with severity of visual field loss in the better eye.

Depression was not significantly associated with age ($P = 0.13$), sex ($P = 0.45$), education ($P = 0.06$), current

working status ($P = 0.07$), widowed ($P = 0.24$), visual acuity ($P = 0.59$), visual field loss ($P = 0.90$), and type of glaucoma ($P = 0.25$) in persons with glaucoma in the study population but was significantly associated with insufficient monthly earnings to meet expenses ($P = 0.005$). Anxiety was not significantly associated with age ($P = 0.38$), sex ($P = 0.26$), current working status ($P = 0.71$), visual acuity ($P = 0.64$), visual field loss ($P = 0.53$), and type of glaucoma ($P = 0.57$) in persons with glaucoma in the study population but was significantly associated with lower education levels ($P = 0.02$), widowed ($P = 0.004$) status, and insufficient monthly earnings to meet expenses ($P = 0.001$). The severity of depression ($P = 0.49$) and anxiety ($P = 0.57$) were not associated with the number of glaucoma medications or the use of timolol or similar betablockers ($P = 0.62$ for depression and $P = 0.34$ for anxiety).

Table 3: Comparison of the PHQ9, GAD-7, ADL scores, and glaucoma quality of life scores between persons with glaucoma and normal controls in the study

	Normal	Glaucoma	P
Patient Health Questionnaire-9			
No depression	125 (83.33%)	95 (64.19%)	One-way ANOVA P<0.001
Mild depression	20 (13.33%)	31 (20.95%)	
Moderate depression	5 (3.33%)	12 (8.11%)	
Severe depression	0 (0.00%)	10 (6.76%)	
Generalized Anxiety Disorder-7			
No anxiety	132 (88.00%)	111 (75.00%)	One-way ANOVA P=0.007
Mild anxiety	14 (9.33%)	24 (16.22%)	
Moderate anxiety	4 (2.67%)	7 (4.73%)	
Severe anxiety	0 (0.0%)	6 (4.05%)	
Activity of Daily Living score (Mean±SD)	14.45±2.33	14.21±3.26	t-test P=0.45
Glaucoma Quality of Life score (Mean±SD)	18.86±4.46	27.5±12.82	t-test P<0.001

Table 4: Comparison of the PHQ9, GAD-7, ADL scores, and glaucoma quality of life scores between persons with POAG and PACG in the study

	Primary Angle Closure Glaucoma (n=66)	Primary Open Angle Glaucoma (n=82)	P
Patient Health Questionnaire-9			
No depression	39 (59.09%)	56 (68.29%)	One way ANOVA P=0.24
Mild depression	16 (24.24%)	15 (18.29%)	
Moderate depression	4 (6.06%)	8 (9.76%)	
Severe depression	7 (10.61%)	3 (3.66%)	
Generalized Anxiety Disorder-7			
No anxiety	48 (72.73%)	63 (76.83%)	One-way ANOVA P=0.02
Mild anxiety	8 (12.12%)	16 (19.51%)	
Moderate anxiety	4 (6.06%)	3 (3.66%)	
Severe anxiety	6 (9.09%)	0 (0.00%)	
Activity of Daily Living score (Mean±SD)	14.50±3.84	13.98±2.07	t-test P=0.33
Glaucoma Quality of Life score (Mean±SD)	28.17±13.88	26.96±11.95	t-test P=0.57

Discussion

Glaucoma is a silent progressive disease with visual acuity and field loss that can affect the quality of vision, social life, and psychosocial behavior of the individual. More than one-third (35.81%) and one-fourth (25.0%) of persons with glaucoma in our study had depression and anxiety, respectively. The quality of life was significantly lower ($P < 0.001$) in persons with glaucoma compared to persons without glaucoma; however, the activities of daily life did not differ significantly between persons with glaucoma and normal persons. We did not find a significant difference in depression, quality of life, and activities of daily living by the type of glaucoma, but moderate to severe anxiety was significantly higher in persons with PACG.

We found several demographic factors that can influence depression and anxiety, such as current working status, economic status, and separation/widowhood, to be significantly more in persons with glaucoma compared to the normal population. Just over half (54.73%) of the persons with glaucoma in our study were males, and we did not find a significant gender difference among persons with glaucoma in this study. A previous study from south India by Kumar *et al.* had reported

that 63% of their study population were males.^[12] However, several other studies have reported that the distribution of glaucoma is more in females. The lack of a gender difference in our study population may be reflective of the equal access to healthcare facilities in Kerala as this was a hospital-based study and not a population-based study. Persons with glaucoma were older than normal in our study and reflects the increasing prevalence of the disease with age. Most of the study population were educated and hence able to self-administer the screening instruments. Persons with glaucoma were less likely to be currently working compared to the normal population and hence more likely to be worried about sufficient monthly income to meet expenses. The proportion of widowed or separated persons was 12.6% among persons with glaucoma and is similar to the 8% reported in a previous study by Kalyani *et al.*^[13]

We found a prevalence of 20.9% for mild depression, 8.1% for moderate, and 6.7% for severe depression in our study, which is similar to a previous study by Agorastos *et al.*^[18] that reported a prevalence of 24.4% for mild, 9.3% for moderate, and 2.3% for severe depression among glaucoma patients. The overall prevalence of depression (35.81%) in persons with glaucoma was not significantly different from a study by Lim

N C *et al.*^[19] from Singapore that reported a prevalence of 30% in persons with glaucoma. Insufficient monthly earning was significantly associated with depression and anxiety in this study, and lower educational levels and widowed or separated status were additionally associated with anxiety. These associations with anxiety and depression are possibly related to the social support network and worries about long-term healthcare expenditure.

Depression and anxiety were not associated with the visual acuity or visual fields in the better or worse eye in this study. The lack of association with actual visual acuity and fields suggests the possibility that depression and anxiety are related to the anticipation or perception of deteriorating vision and field loss rather than the actual visual acuity or field status. Previous studies have reported similar results, including in patients with one eye blindness from glaucoma.^[20-22] Holló G *et al.* reported a higher risk of anxiety, depression, hopelessness about the future, and decreased self-assessments of general health in glaucoma patients with good visual acuity and visual functions of the fellow eye with no risk of future visual impairment.^[21] Rulli *et al.*^[22] reported that psychological alterations in persons with glaucoma can occur with an actual decline in the visual functions and may also occur by the possibility of future functional decline or glaucomatous progression.

There was no significant difference in the prevalence of depression between POAG and PACG but the levels of depression were significantly higher in PACG patients (40.9%) than in POAG patients (31.70%) in our study. There was a significant difference in the anxiety levels of PACG (27.2%) compared to POAG (16%), $P = 0.02$, which is consistent with results from a previous study from China.^[23]

There are conflicting reports in the literature on the association of topical β -blockers and depression. Bali *et al.*^[24] reported that patients on topical β -blockers were 4.9 times more likely to have depression as compared with normal controls, whereas other studies^[25,26] did not find any increased risk of depression. We did not find any significant association between the use of topical β blockers/prostaglandin analogs and depression or anxiety in our study. We also did not see any significant association for depression or anxiety with the mean number of glaucoma medications used in persons with glaucoma in the study. The fear of loss of vision and visual fields, loss of functional activity, and possible side effects of treatment can lead to depression. We found that persons with glaucoma reported greater difficulty in routine daily activities and sadness compared to the normal study population, which is consistent with the results from previous studies worldwide.

Redundant retinal oxidative stress, which leads to extensive loss of intrinsically photosensitive retinal ganglion cells (ipRGCs), is one of the pathophysiological mechanisms of glaucomatous optic nerve damage.^[27] These ipRGCs have a major role in nonvisual phototransduction through the retinohypothalamic tract to the suprachiasmatic nucleus (SCN) and in the regulation of the pineal gland and melatonin.^[28,29] Thus, glaucoma affects the photo-dependent circadian rhythm alterations and melatonin production. Studies on circadian rhythm misalignment have shown a close relation between sleep disorders and depression.^[30] This misalignment of chronoreceptors is relatively associated with retinal ganglion cell death.^[31] While neuropsychiatric

studies by Agorastos *et al.*^[18] suggested a relation of visual field defect and depression and anxiety in glaucoma patients, the results of our study suggest that visual impairment is not a sole factor for the development of mental health problems in persons with glaucoma. We hypothesize that depression and glaucoma are related directly irrespective of visual acuity or field defects and can relate to the theory of chronodisruption. However, we need to study this possible relation further with larger samples and diverse populations.

The overall prevalence of anxiety (18.46%) in our study population is comparable to the prevalence of generalized anxiety disorder in India as reported by Reddy and Chandrashekar *et al.*,^[32] which found anxiety in 20.7% (18.7%–22.7%) of the general population of India. We found a prevalence of 25% anxiety in persons with glaucoma, including mild anxiety (16.22%), moderate (4.73%), and severe anxiety (4.05%).

Glaucoma influences the quality of life similar to other chronic systemic diseases such as diabetes and dementia.^[33] The Glaucoma quality of life (GQOL) scores were significantly higher compared to the normal population, indicative of a reduced quality of life in persons with glaucoma. Reduced QoL in glaucoma patients has been reported earlier in a cross-sectional study by Sherwood *et al.*,^[34] and we found similar results. The reduction in QoL was significant after adjusting for clinic-demographic factors in a multivariate linear regression model. The reduced QoL may be impacted by the depression, anxiety, and reduction in functional activities associated with glaucoma that may be influenced by the perception or possibility of loss of vision rather than actual loss of vision.

The lack of association with ocular clinical factors such as visual acuity, fields, type of glaucoma, and medications suggests that targeted high-risk-subgroup screening of persons with glaucoma is not feasible. The high prevalence of depression, anxiety, and reduced QoL indicates that it may be necessary to screen all persons with glaucoma for anxiety and depression. The PHQ-9 and GAD questionnaires are easily available, easy to administer, do not take much additional time, and can be self-administered and scored immediately.

To our knowledge, this is the first study in South India to report the prevalence of depression and anxiety among patients with glaucoma using validated scales such as PHQ-9 and GAD-7. The questionnaires were self-administered, minimizing the possibility of prompted responses. All subjects had a detailed ophthalmic examination and diagnosis of glaucoma. However, the cross-sectional study design does not allow us to comment on possible causal relations between glaucoma, depression, and anxiety. The single-center nature of the study and the hospital-based design are limitations that limit the generalization of the results to a larger population due to the possibility of selection bias. The PHQ-9 and GAD-7 are screening instruments and we have not correlated the diagnosis by screening with clinical diagnosis after a psychiatry consultation in this study. The study overlapped with the COVID-19 pandemic and the first lockdown, and we do not know how or if that possibly influenced the estimates of depression and anxiety in this population.

Conclusion

The higher prevalence of depression and anxiety in persons with glaucoma may necessitate the integration of screening protocols using PHQ and GAD scales to identify persons at risk for depression and anxiety. The lack of ophthalmic risk factors associated with depression and anxiety emphasizes the importance of psychological evaluation and combined management with a psychiatrist in glaucoma management. Further studies on the cumulative probability of visual field and visual acuity loss in persons with glaucoma may help in more focused counseling and may reduce anxiety and depression associated with a perceived possibility of vision impairment and blindness.

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Conflicts of interest

There are no conflicts of interest.

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