


# BMJ Open Use of the Patient Health Questionnaire-9 (PHQ-9) and Generalized Anxiety Disorder-7 (GAD-7) questionnaires for clinical decision-making and psychological referral in ophthalmic care: a multicentre observational study

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## ABSTRACT

**Objectives** The aim of this study was to evaluate the influence of anxiety and depression on clinician decision-making in patients suffering from chronic eye disease in ophthalmological clinical practice.

**Design and setting** This multicentre observational study, in collaboration with the WHO, included ophthalmologists and their patients affected by chronic eye disease. States of anxiety and depression were screened with specific questionnaires, the Patient Health Questionnaire-9 (PHQ-9) and Generalized Anxiety Disorder-7 (GAD-7), self-administered by patients before the visit. In the present analysis, we report data from three major eye care centres in Italy between 2021 and 2022.

**Primary and secondary outcomes** To assess self-reported changes in ophthalmologists' clinical approach (communication style and their clinical-therapeutic strategies) and decisions after knowing questionnaire scores (primary aim), and to analyse the PHQ-9 and GAD-7 scores in patients with chronic eye diseases (secondary aim).

**Results** 41 ophthalmologists and 359 patients were included. The results from PHQ-9 and GAD-7 scores showed critical depression and anxiety status scores (PHQ-9  $\geq 5$  and GAD-7  $\geq 10$ ) in 258 patients. In 74% of cases, no actions were taken by the ophthalmologists based on these scores; in 26% of cases, they changed their clinical approach; and in 14% of cases, they referred the patients for psychological/psychiatric evaluation.

**Conclusions** States of anxiety and depression affect many patients with chronic eye conditions and need to be detected and managed early to improve patients' well-being. Providing ophthalmologists with knowledge of their patients' psychological conditions can change the clinical management and attitude towards referral for a psychological evaluation. Further studies are needed to expand our knowledge of how

## STRENGTHS AND LIMITATIONS OF THIS STUDY

- ⇒ This study was part of an international initiative based on the same protocol, allowing future comparative studies on the burden of anxiety and depression in people with vision impairment in different settings worldwide.
- ⇒ A strength of our study was the multicentre data collection and the inclusion of a large number of clinicians, including different subspecialties, which could improve the generalisability of our findings.
- ⇒ Among the limitations, we excluded some patients who could not sign the informed consent and self-administer the questionnaires due to severe vision impairment, which may have reduced the spectrum of depression and anxiety severity in our sample.

to raise awareness among ophthalmologists regarding multimorbidity of patients suffering from chronic eye diseases in order to achieve better clinical outcomes.

## INTRODUCTION

Chronic eye diseases affect people of all ages and sociocultural backgrounds, although they can be found most commonly among people aged 50 years and over.<sup>1,2</sup> Common eye conditions in this age group are age-related macular degeneration (AMD), diabetic retinopathy (DR), glaucoma and inherited retinal dystrophies.<sup>2-4</sup>

A deterioration in quality of life has been reported in people suffering from chronic eye diseases.<sup>5-7</sup> This general status could

influence and/or be influenced by mental status.<sup>5</sup> In fact, a prevalence of 25% of depression and about 10–30% of anxiety has been estimated in patients with chronic eye disease.<sup>8–10</sup> A recent prospective study<sup>11</sup> reported that the incidence of subthreshold depression and anxiety in older adults with vision impairment is twice as high compared with older adults in general. These data confirm previous data reporting an increased risk of 1.6 and 1.5 times for anxiety and depression, respectively, in patients with vision impairment compared with people without visual problems.<sup>12</sup>

Several mechanisms have been proposed to explain the development of depression and anxiety among patients with visual loss,<sup>13</sup> including the relationship between loss of functional capacity and depression symptoms, deficit in problem-solving skills and alteration of ‘control strategy’. The main factors affecting quality of life, particularly in older people, include not only vision impairment, but also the presence of systemic comorbidities, ageing processes, social impact (stigmatisation) due to visual disability, decline in family income and isolation, leading to an increased risk of mental health problems.<sup>5 7 14–16</sup>

Finally, low medication adherence was found in older adults with chronic illnesses who have low social support, high levels of depression, and poor knowledge of medication and self-efficacy.<sup>7</sup> This poor adherence to therapy in chronic patients leads to crucial medical and social disadvantages.<sup>7 11 13 17 18</sup> Mental health conditions affect and are affected by chronic physical diseases. They can be precursors of one another, consequences or the result of interactive effects. Conversely, people with chronic diseases are put under physical and psychological stress that can trigger the onset of depression or anxiety. The multiple links between mental health conditions and other chronic diseases mean they often co-occur.

A recent review<sup>16</sup> reported that depression and anxiety for individuals with progressive vision loss may be experienced before further vision decline, and a concomitant condition of vision impairment and depression may result in greater disability than either condition alone. Interestingly, the authors reported that vision-specific distress increased the risk of depression and was independent of visual acuity (VA); in fact, patients with newly diagnosed glaucoma (20 of 40 or better VA) experienced some vision-related tasks associated with depressive symptoms (but VA measurement was not correlated with depression scores). Among patients with neovascular AMD, 56% had anxiety regarding intravitreal injection treatment, 3.3% of cases due to injection pain, and mostly due to potential complications and treatment efficacy, independent of the number of injections.<sup>16 19</sup>

Evidence collected in a systematic review has shown that psychological therapies and/or group programmes may be effective in improving quality of life of people with low vision.<sup>20</sup>

A missed diagnosis of subthreshold mental disorders in chronic patients could lead to poor adherence to

the therapeutic pathway,<sup>10 13 21</sup> which would mean fewer chances of improving/stabilising vision, with a potential reduction in quality of life, increased risk of developing other comorbidities, loss of productivity, increased healthcare costs, increased burden of care and number of visits.<sup>22 23</sup>

Despite this evidence, there is no standard methodology for assessing mental status in patients with chronic eye conditions, in contrast with the widely recognised need for early detection and management of mental health problems.<sup>10 11 18</sup>

To improve the well-being of patients (physical and psychological), the WHO has created an international collaborative network to promote comprehensive eye care including mental health for people living with vision impairment. A US-based report by this network found that providing ophthalmologists with information on the mental health status of their patients may lead to changes in their clinical approach and referral pattern.<sup>18</sup> As members of this network, we shared the same protocol to replicate the study in the Italian setting.

This study also aimed to report the level of anxiety and depression in the same population of patients with chronic eye disease, using the Patient Health Questionnaire-9 (PHQ-9) and Generalized Anxiety Disorder-7 (GAD-7) questionnaires, since this information is lacking in our setting.

## METHODS

In the present study, we report data from three major eye care centres in Italy (Ophthalmology Unit, ‘A Gemelli IRCCS University Hospital Foundation’, Rome; Institute of Ophthalmology, S Raffaele Hospital, Milan; and IRCCS–Fondazione Bietti, Rome), enrolling patients affected by chronic eye diseases between 2021 and 2022. The data collection was part of a multicentre observational international study, promoted by the WHO and coordinated by the Italian National Reference Centre for the Prevention of Blindness and Rehabilitation of the Visually Impaired, WHO Collaboration Center for Vision Rehabilitation and Blindness Prevention, that involved several centres across the world. This study adhered to the Declaration of Helsinki and was approved by the Ethics Committee of the ‘Agostino Gemelli’ University Hospital Foundation IRCCS, Rome, Italy. Written informed consent was obtained from all participants.

## Study population

The study population included: (1) ophthalmologists in general units or specialised in medical retina, glaucoma and anterior segment attending patients with chronic eye disease (excluding residents and emergency ophthalmologists); and (2) patients referred to their units for chronic eye diseases that satisfied the following inclusion criteria: age ≥18 years; chronic eye diseases such as AMD, DR, degenerative myopia, inherited retinal diseases, glaucoma, corneal disease, inflammatory eye disease and

dry eye syndrome; and possibility/capability to sign the study informed consent. Exclusion criteria were patients with manifestation of and/or previously diagnosed with cognitive impairment, and inability to sign the informed consent and to self-administer the questionnaires due to severe vision impairment. The ophthalmologists were equally recruited between involved centres. The patients' recruitment was consecutive until the sample size was reached.

### Primary and secondary outcomes

The primary aim was to evaluate the effect of being aware of people's levels of anxiety and depression in the clinical management and interaction during consultation for chronic eye disease. States of anxiety and depression were measured with specific questionnaires: PHQ-9 and GAD-7,<sup>18</sup> and reported to ophthalmologists. The secondary aim was to analyse the PHQ-9 and GAD-7 scores in patients with chronic eye diseases.

PHQ-9 and GAD-7 questionnaires were internationally validated to assess emotional well-being status: PHQ-9 scores above 5, 10, 15 and 20 are classified as mild, moderate, moderately severe and severe depression, respectively; GAD-7 scores above 5, 10 and 15 are classified as mild, moderate and severe anxiety, respectively.<sup>18 24</sup> Of note, for this study, we have decided that a PHQ-9  $\geq 5$  and GAD-7  $\geq 10$  scores require referral of patients for psychological evaluation and that for scores PHQ-9  $\geq 15$  and GAD-7  $\geq 15$ , a psychiatric evaluation was indicated. We have adapted the recommendation for psychological referral for depression to cases with lower scores ( $\geq 5$  for PHQ-9) in order to challenge clinicians with milder cases of depression. In fact, it is known that the sensitivity of PHQ-9 is only around at 50% of cut-off  $\geq 10$ .<sup>25</sup>

### Study design and procedure

As a first step, patients received two screening questionnaires for depression (PHQ-9) and for anxiety (GAD-7) and a short data collection form collecting information on age, gender, education, eye disease and time since diagnosis (variables also reported in table 1). The questionnaires were self-administered while patients were waiting for their ophthalmological examination. The PHQ-9 and GAD-7 scores were evaluated by the ophthalmologists, who were invited to recommend clinical psychologist or psychiatric visit in case of scores exceeding cut-off values. The ophthalmologists were instructed on the questionnaires' scores when they accepted to participate in our study; nonetheless, we wanted to investigate the effect of becoming aware of the issues of depression and anxiety on clinical decision-making in this regard, without making referral a mere compulsory action related to fixed thresholds for normality.

In the second step, the ophthalmologists filled two specifically developed questionnaires: the first one was filled out only once, at the end of the study, to understand their opinion on depression and anxiety, and the second

**Table 1** General characteristics of the 359 patients included in the study

	n (%)
Age range (years)	
18–39	21 (5.8)
40–59	85 (23.7)
60–80	253 (70.5)
Sex	
Male	175 (48.7)
Female	184 (51.3)
Education	
Elementary	46 (12.8)
Primary	130 (36.2)
Secondary	130 (36.2)
University	53 (14.8)
Ocular disease	
Aged-related macular degeneration	212 (59.0)
Stargardt disease	3 (0.8)
Glaucoma	40 (11.2)
Inflammatory diseases	31 (8.6)
Retinitis pigmentosa	11 (3.1)
Diabetic retinopathy	62 (17.3)
Time since diagnosis (years)	
0–2	75 (20.9)
2–5	122 (34)
>5	162 (45.1)

one was completed at the end of the clinical examination for each included patient, to evaluate their own approach and report on whether their communication with the patient and their clinical-therapeutic strategies had been influenced by the patient's state of anxiety and depression as recorded in the questionnaires. For the questionnaires, please refer to table 2.

### Data collection and management and statistical analysis

All variables were collected in a spreadsheet (Excel). All patients' and ophthalmologists' data were anonymised. Binary or categorical variables were presented as percentages, whereas continuous variables as means and SDs.

Given that the expected prevalence of anxiety and depression in the general population for the chronic ocular diseases under study, such as AMD, glaucoma, DR, degenerative myopia and clinically detectable dry eye syndrome, can range from 0.35% to 0.85% of the general population (meaning from 350 individuals to 850 per 100 000), we considered the following sample size calculation:

Given:

$$n = [t^2 P(1 - P)] / D^2$$

where:

► n=sample size



**Table 2** Ophthalmologists' questionnaires

First questionnaire	Ophthalmologists (n=41)
Q1. In your clinical practice, do you pay attention to anxiety and depression in the global assessment of the patient?	Yes: 40 (98.0%) No: 1 (2.0%)
If no, why?	n=1 (2%)
a. It is not part of my training	None
b. I do not know the consequences of adherence to the prescribed therapy	None
c. In my workplace, the service of psychology/psychiatry is not present	None
Q2. Do you think it would be useful for ophthalmologists to have specific training in knowing how anxiety and depression affect adherence to treatment?	Yes: 37 (90.0%) No: 4 (10.0%)
Q3. Overall, in your opinion, the use of the PHQ-9 is:	Useful: n=37 (90.0%) Useless: n=4 (10.0%)
Q4. Overall, in your opinion, the use of the GAD-7 is:	Useful: n=37 (90.0%) Useless: n=4 (10.0%)
Second questionnaire	Overall 359 patients
Q1. Did you use the scores from the questionnaires to change your clinical approach for this patient today? (reported per patient)	Yes: 94 (26.0%) No: 265 (74.0%)
Q2. Did you modify the choice of treatment based on the scores? (reported per patient)	Yes: 1 (0.3 %) No: 358 (99.7%)
Q3. Did you modify the follow-up protocol/frequency? (reported per patient)	Yes: 1 (0.3%) No: 358 (99.7%)
Q4. Did you change your communication style with the patient following the scores from the questionnaire? (reported per patient)	Yes: 92 (25.6%) No: 267 (74.4%)
Type of changes in communication strategy	
None	N=267 (74.0%)
More time listening to the patient	N=55 (16.0%)
Gave more information to the patient	N=37 (10.0%)

GAD-7, Generalized Anxiety Disorder-7; PHQ-9, Patient Health Questionnaire-9.

- ▶  $t$ =distribution
- ▶  $P$ =prevalence in the target population
- ▶  $D$ =desired absolute precision

Also equivalent to:

$$n > \pi (1 - \pi) [2Z_{\alpha/2}/\delta]^2$$

where:

- ▶  $n$ =sample size
- ▶  $z_{\alpha/2}$ =1.96 for  $\alpha=5\%$
- ▶  $\pi$ =known prevalence in the general population (0.35%)
- ▶  $\delta$ =maximum acceptable width of the CI

Data were presented as cross-tabulations for categorical variables, such as questionnaire scores or ophthalmologists' decision-making. For inferential evaluations, associations of covariates with overall questionnaire score or the decision to refer the patients were investigated with ordinal or standard logistic regression, as appropriate. Logistic regression was used to compute the OR (95% CI) of referral by ophthalmologists for demographic variables (age, sex, education) and PHQ-9 or GAD-7 score. Univariate associations were obtained, followed by separate association with PHQ-9 and GAD-7 scores adjusted

by educational level. We assessed model fit using a goodness-of-fit (Hosmer and Lemeshow) test, which was never statistically significant, indicating acceptable fit.

Stata V.18.0 (StataCorp, College Station, Texas) was used as statistical package.

## Patient and public involvement

None.

## RESULTS

### Ophthalmologist and patient characteristics

41 ophthalmologists (19 female and 22 male) were included in this study. About half (51.2%) were aged 30–39 years, and 48.8% were 40 years or older. 29 of 41 (71%) were retinal specialists, six (15%) were glaucoma specialists, five (12%) were general ophthalmologists and one (2%) was an anterior segment/inflammatory disease specialist. 23 of 41 (56.2%) had 0–5 years of ophthalmological experience, 11 (26.8%) had 6–15 years and 7 (17%) had >15 years of clinical practice.

359 patients were enrolled in the study (184 female and 175 male), aged between 18 and 80 years; all

details concerning their age range, education, chronic ocular disease and time since diagnosis are reported in [table 1](#).

The PHQ-9 and GAD-7 scores were as follows: (1) for PHQ-9 questionnaire, 172 patients (48%) scored 0–4, 118 (32.9%) had a score 5–9, 68 patients (19%) scored 10–14 and 1 patient (0.1%) scored  $\geq 15$ ; (2) for GAD-7 questionnaire, 175 patients (48.7%) had a score  $\leq 4$ , 120 patients (33.4%) scored 5–9 and 64 patients (17.9%) scored  $\geq 10$ .

### Impact of patient anxiety and depression on ophthalmologists' clinical approach

Data regarding the primary outcome are reported in [table 2](#). The analysis of ophthalmologists' replies to the first questionnaire showed that almost all took into account the patient's psychological state, since 40 out of 41 participants (98%) in the study answered that they took these aspects into consideration, while only 1 (2%) did not due to inadequate training. The majority of ophthalmologists, 37 out of 41 (90%), considered ad hoc training to be important for their clinical practice. Furthermore, 37 out of 41 (90%) considered the PHQ-9 and the GAD-7 questionnaires useful for their practice, and only 4 (10%) did not consider them helpful.

The analysis of the second questionnaire ([table 2](#)) showed that in 74% of cases, no actions were taken by the ophthalmologists, and in 26% of cases, their approach changed.

Interestingly, the results from PHQ-9 and GAD-7 scores showed depression and anxiety scores higher than the cut-off limit in 258 out of 359 patients (71.9%) (194 for PHQ-9 and 64 for GAD-7) and critical levels of both anxiety and depression (PHQ-9  $\geq 5$  and GAD-7  $\geq 10$ ) in 58 patients (22.3% of those to be referred for psychological evaluation), resulting in 264 referable patients above threshold for either or both questionnaires (73.5%). [Tables 2](#) and [3](#) show the modifications to clinical approach based on questionnaire scores; specifically, a change in the treatment plan was reported in one case, while a change in visit frequency was considered in another case. With 92 patients (25.6% of cases), the ophthalmologists changed

their communication approach in terms of more time spent listening to the patients (55 cases, 16%) and giving more information to the patient (37 cases, 10%).

In 14% of cases (49 out of 359 patients), the ophthalmologists referred the patients for psychological/psychiatric evaluation, whereas in 86% of cases (310 cases), no psychological in-depth visit was required for the following reasons: score within normal ranges (215 cases) and decision to monitor the patient until the next ophthalmological visit (95 cases).

### Factors associated with PHQ-9 and GAD-7 scores and referral patterns

The analysis of variation of referral among different ophthalmologists is detailed in [table 4](#) and in [figure 1](#).

[Table 4](#) shows univariable associations of each categorical covariate with being referred for psychological assessment by ophthalmologists. Since only education (at primary level) was associated with referral, two further multivariable models assessed the association of either PHQ-9 or GAD-7 with referral while adjusting for education. No change in ORs was observed in adjusted versus unadjusted models, as could be expected.

The analysis of questionnaire score revealed that 194 patients for PHQ-9 (score  $\geq 5$ ) and 64 patients for GAD-7 (score  $\geq 10$ ) should have been referred for psychological evaluation, but only 32 patients for PHQ-9 (17%) and 17 patients for GAD-7 (27%) were effectively referred (online supplemental figure 1A,B).

Multivariate associations of patients' characteristics with PHQ-9 and GAD-7 scores are reported in the online supplemental table 1. Of note, patients aged 40 years and older were less likely to have both anxiety and depression than those aged 30–39 years. Females were more likely to have anxiety than males, and this pattern also approached significance for depression. Compared with having elementary school education, patients with higher education levels had lower depression scores, and this pattern was confirmed for anxiety with borderline significance for those with secondary and university education.

**Table 3** Modification in clinical approach based on GAD-7 and PHQ-9 scores

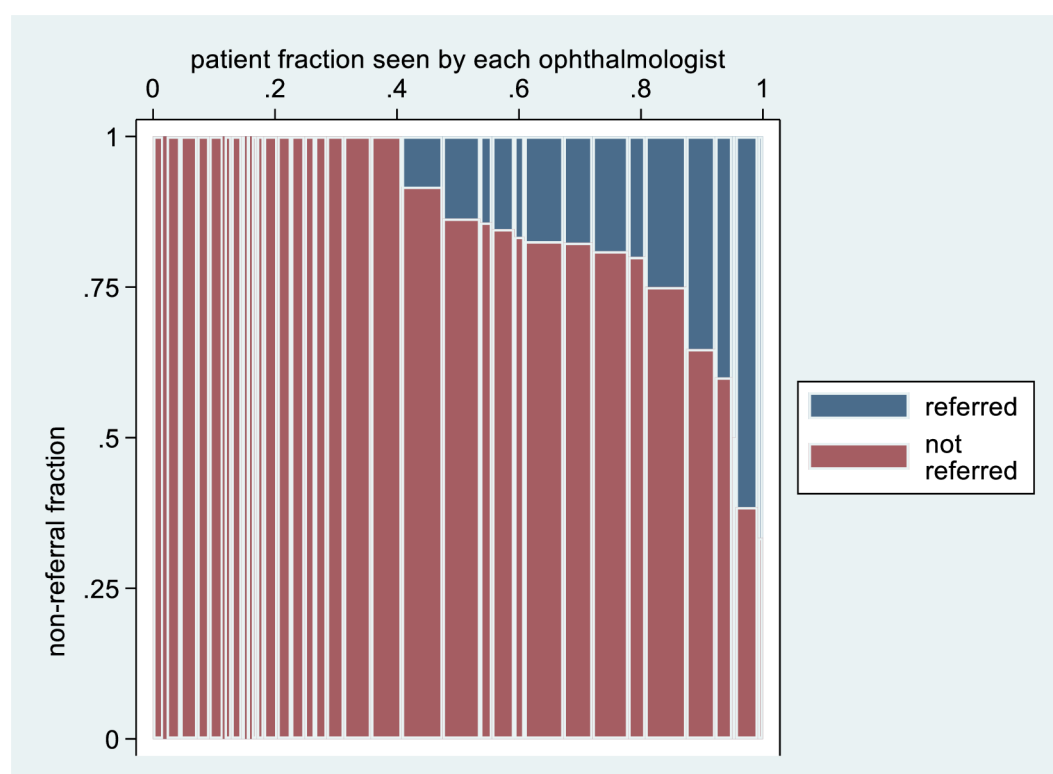
Modification of clinical approach	GAD-7 score (anxiety-level evaluation)			
	0–4 (minimal)	5–9 (mild)	$\geq 10$ (moderate)	
Yes	38 (21.7%)	32 (26.7%)	24 (37.5%)	94 (26.2%)
No	137 (78.3%)	88 (73.3%)	40 (62.5%)	265 (73.8%)
Overall	175	120	64	359
Modification of clinical approach	PHQ-9 score (depression-level evaluation)			
	0–4 (minimal)	5–9 (mild)	$\geq 10$ (moderate)	
Yes	38 (23%)	29 (23.8%)	27 (37.5%)	94 (26.2%)
No	127 (77%)	93 (76.2%)	45 (62.5%)	265 (73.8%)
Overall	165	122	72	359

GAD-7, Generalized Anxiety Disorder-7; PHQ-9, Patient Health Questionnaire-9.

**Table 4** Association with being referred for psychological assessment

Covariate	Univariate OR	P value	Multivariate OR PHQ-9	P value	Multivariate OR GAD-7	P value
Age						
30–39	Reference					
40–59	0.63 (0.18, 2.23)	0.475				
>60	0.66 (0.21, 2.09)	0.482				
Female (vs male)	1.38 (0.75, 2.56)	0.303				
Education level						
Elementary	Reference		Reference		Reference	
Primary	5.50 (1.25, 24.2)	0.024	9.52 (2.04, 44.6)	0.004	6.94 (1.50, 32.1)	0.013
Secondary	3.54 (0.79, 15.9)	0.099	5.70 (1.20, 27.1)	0.029	4.33 (0.92, 20.4)	0.064
University	1.35 (0.22, 8.44)	0.750	2.90 (0.43, 19.8)	0.277	1.69 (0.26, 11.2)	0.587
PHQ-9						
0–4	Reference		Reference			
5–9	3.15 (1.23, 8.07)	0.017	3.30 (1.27, 8.57)	0.014		
≥10	16.0 (6.53, 39.2)	<0.001	18.6 (2.03, 27.1)	<0.001		
GAD-7						
0–4	Reference				Reference	
5–9	3.94 (1.58, 9.82)	0.003			4.17 (1.65, 10.5)	0.002
≥10	15.3 (6.12, 37.9)	<0.001			16.4 (6.50, 41.4)	<0.001

GAD-7, Generalized Anxiety Disorder-7; PHQ-9, Patient Health Questionnaire-9.

**Figure 1** Variation in referral between different ophthalmologists via random-effects logistic regression. Each vertical bar refers to each ophthalmologist and its width is proportional to the number of patients seen. No patient was referred by 40% of the ophthalmologists.

The education level was the only demographic variable showing association with being referred.

Finally, we investigated the variation of referral between different ophthalmologists. Figure 1 shows that 40% of the ophthalmologists, especially those with a lower volume of visits, did not refer any patient, whereas the others referred from about 10% to 60% of their patients with significant PHQ-9 and GAD-7 scores.

## DISCUSSION

We aimed to investigate whether the psychological state of patients attending eye consultations for chronic disease was taken into account by ophthalmologists and/or could influence the ophthalmologists' approach. Using PHQ-9 and GAD-7 questionnaires, we have also reported the level of anxiety and depression in the same population of patients with chronic eye disease. For this purpose, we adopted a WHO-sponsored protocol which has already been used in the USA.<sup>18</sup>

We found that 258 of 359 patients presented scores of anxiety and depression higher than the cut-off values (PHQ-9  $\geq 5$  and GAD-7  $\geq 10$ , mild depression and moderate anxiety). Similar findings have been reported by several other studies,<sup>8–11 13</sup> suggesting that the trigger for this state of anxiety and depression could be their chronic disease itself.

Our analysis of ophthalmologists' responses showed that 98% of enrolled specialists reported paying attention to the state of anxiety or depression of ophthalmic outpatients and considered the PHQ-9 and GAD-7 questionnaires to be useful tools. Despite this evidence and their awareness of the importance of this topic, only 26% of ophthalmologists enrolled in this study used the questionnaire scores to change their clinical approach during visits (table 2, second questionnaire, Q1); in 99.7% of cases, no change in treatment or protocol or frequency of visits was reported (table 2, second questionnaire, Q2) and only 25.6% of them changed their communication style (table 2, second questionnaire, Q4). Our data are in line with the previous study using our same study methodology and psychological questionnaires.<sup>18</sup> In fact, Naufal *et al*<sup>18</sup> found that 27% of patients had mild-moderate anxiety or depression, and 2% had suicidal thoughts; in response to this, ophthalmologists opted to change their clinical approach (28%) and their communication style (31%).

Additionally, the analysis of the number of patients with questionnaire scores higher than the cut-off value (ie, patients to be referred to psychologists or psychiatrists) and the number of patients effectively referred by the ophthalmologists for an in-depth psychological evaluation yielded interesting results. The number of patients referred for further diagnostic investigation was small compared with those who needed it, especially in the sample of patients where the scores of both questionnaires were higher than the cut-off threshold; this is of particular relevance as not referring to psychological

specialists, when needed, could increase the risk of developing mental disability in addition to chronic eye disease, thus resulting in a double disability (visual and mental).<sup>5 11</sup>

While this could mean that a more explicit research protocol could have been required, it also highlights the challenges in implementing these tools in everyday clinical practice, given the high rate of eye care patients presenting with mental health issues.

There is uncertainty as to why ophthalmologists said they pay attention to the psychological condition of their patients and found the screening questionnaires for anxiety and depression to be very useful, but then did not use the results consistently to refer the patient for in-depth psychodiagnostics or did not change their clinical approach. As a result, further investigations are needed and focus group discussions involving doctors and patients could provide an answer to this question. We infer that the awareness of the possible large number of referrals generated using PHQ-9 and GAD-7 cut-offs might have played a role, as the ophthalmologists were aware of the limited mental healthcare resources in the health system and in their institutions. Nonetheless, there was wide variation in referral rate and at least the higher cut-off grading, implying more severe disease, would warrant strong recommendation for referral, but would also need to be incorporated in clinical care pathway and included in the monitoring of patient flow, resource use and possibly health outcomes.

From the analysis of our results, it emerged that ophthalmologists with a low volume of patients were less likely to refer their patients. Several data reported that increasing patient volume was associated with improved patient outcomes.<sup>26 27</sup> It might be thought that ophthalmologists with low-volume patients could have more time to spend with their patients during the consultation (facilitator); however, our data would suggest that ophthalmologists with low-volume patients might have less experience and lack confidence in dealing with patients with chronic eye disease to also manage possible mental health problems or consider them, thus representing a barrier for these patients.

Another issue could be that ophthalmologists considered themselves not adequately trained for psychological evaluation and thought that specific training in knowing how anxiety and depression affect adherence to treatment could be useful. Furthermore, a high number of ophthalmologists were aware that training in knowing the effects of anxiety and depression states on chronic patients and the use of screening tools is important for their clinical practice but not adequately covered during their medical studies. This lack of education on the provision of comprehensive care, which is on the basis of the current approach of people-centred service provision, could increase direct and indirect (caregivers) costs due to the development of double-disease burden, while also reducing treatment efficacy due to poor compliance of chronic patients also suffering from mental conditions.<sup>7 10</sup> A recent article by van Munster *et al*,<sup>21</sup> focusing

on visually impaired patients, reported the difficulties in acknowledging the effects of concomitant mental health problems on patients' vulnerability and inequality as well as the potential facilitator role of healthcare providers recognised by the patients themselves. Despite this evidence, the study<sup>21</sup> also highlighted the lack of skills and attitude of eye care providers to recognise and discuss this topic with visually impaired patients: indeed, only a quarter of ophthalmologists provided education and information for suspected depression and they often reported their low training in this topic (skills and knowledge) as a barrier to manage visually impaired patients. Interestingly, in our study, we reported a similar approach by ophthalmologists for patients with chronic eye diseases, independently from vision loss, suggesting that psychoeducation should be extended to all eye care and healthcare providers to improve the quality of care.

We found no suggestion of inequality in patient referral by age and gender. However, patients with only primary education were less likely to be referred compared with those with higher education, a marker of socioeconomic status, which could be due to limited self-assertion towards an ophthalmologist or to poor bidirectional communication during the examination, both of which raise equity concerns.

A strength of our study was the multicentre data collection and the inclusion of a large number of clinicians, including some from different subspecialties, which could improve the generalisability of our findings. Moreover, this study was part of an international initiative based on the same protocol, allowing future comparative studies on the burden of anxiety and depression in people with vision impairment in different settings from all over the world. An important strength of our study was the use of screening questionnaires (PHQ-9 and GAD-7) which are easy to use, feasible and can be self-administered by the patients so as to allow easy and early recognition of the presence of mental health problems.

Among the limitations, we excluded some patients who could not sign the informed consent and self-administer the questionnaires due to severe vision impairment. This exclusion may have reduced the spectrum of depression and anxiety severity in our sample. Another limitation was the absence of VA data to correlate the questionnaire scores, but our aim was to promote awareness of mental health diseases in patients with chronic eye disease, not necessarily visually impaired.

Our study highlights an important unmet need for patients to be referred for psychological evaluation, as well as insufficient changes to the clinical approach or communication strategy in the analysis of ophthalmologists' questionnaires. A possible explanation for this could be related to a limitation in treatment choices available to patients with chronic eye disease. In our sample, 13.6% of patients were referred from the ophthalmologist to psychologists or psychiatrists. Naufal *et al*<sup>18</sup> reported rates of referral to social work/psychiatry services of 60%, 3.7% and 0% for patients with moderately severe or worse,

mild-to-moderate or minimal scores, respectively. The variation of referral between different ophthalmologists could suggest that a more directive management protocol should be adopted; it also highlights the difficulty in the implementation of these tools in clinical practice.

### Implication in clinical practice

Taking into account the scores obtained in the questionnaires, the change in the clinical approach was insufficient compared with the number of those who requested it, and the awareness of the patient's psychological aspects mainly resulted in a change in communication. A crucial aspect was that we found a consistent choice in not changing the follow-up schedules, despite the high levels of depression and anxiety scores recorded, which is in sharp contrast with the importance of prevention to counteract any disability resulting from the worsening of eye diseases.

As reported above, this attitude could lead to poor compliance with therapy and healthcare pathways in general, worsening the disability level of patients with chronic eye disease (mental and ocular) and also increasing the costs for caregivers and care. Integrating mental health in health programmes for specific physical diseases or populations has proven to be both feasible and cost-effective, improving both mental and physical health. We suggest that a 'directive' approach, aiming to improve clinical practice, should be part of a larger implementation project adopting new clinical pathways for psychological care, linking different professionals and services and including local guidance for each step of referral.

### CONCLUSIONS

States of anxiety and depression affect many patients with chronic eye conditions and need to be diagnosed and treated at an early stage to improve their well-being. Providing ophthalmologists with knowledge of their patients' psychological conditions can change their clinical management and attitude towards referral for a psychological evaluation. Further implementation studies should investigate how to improve psychological referral and optimise resource use in specific clinical settings.

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SPM, ST, SR and ER. Manuscript drafting—EC, ER, SF and ST. Revision of the manuscript—SPM, GV, SF, ST, ER and MP. SF is responsible for the overall content as the guarantor.

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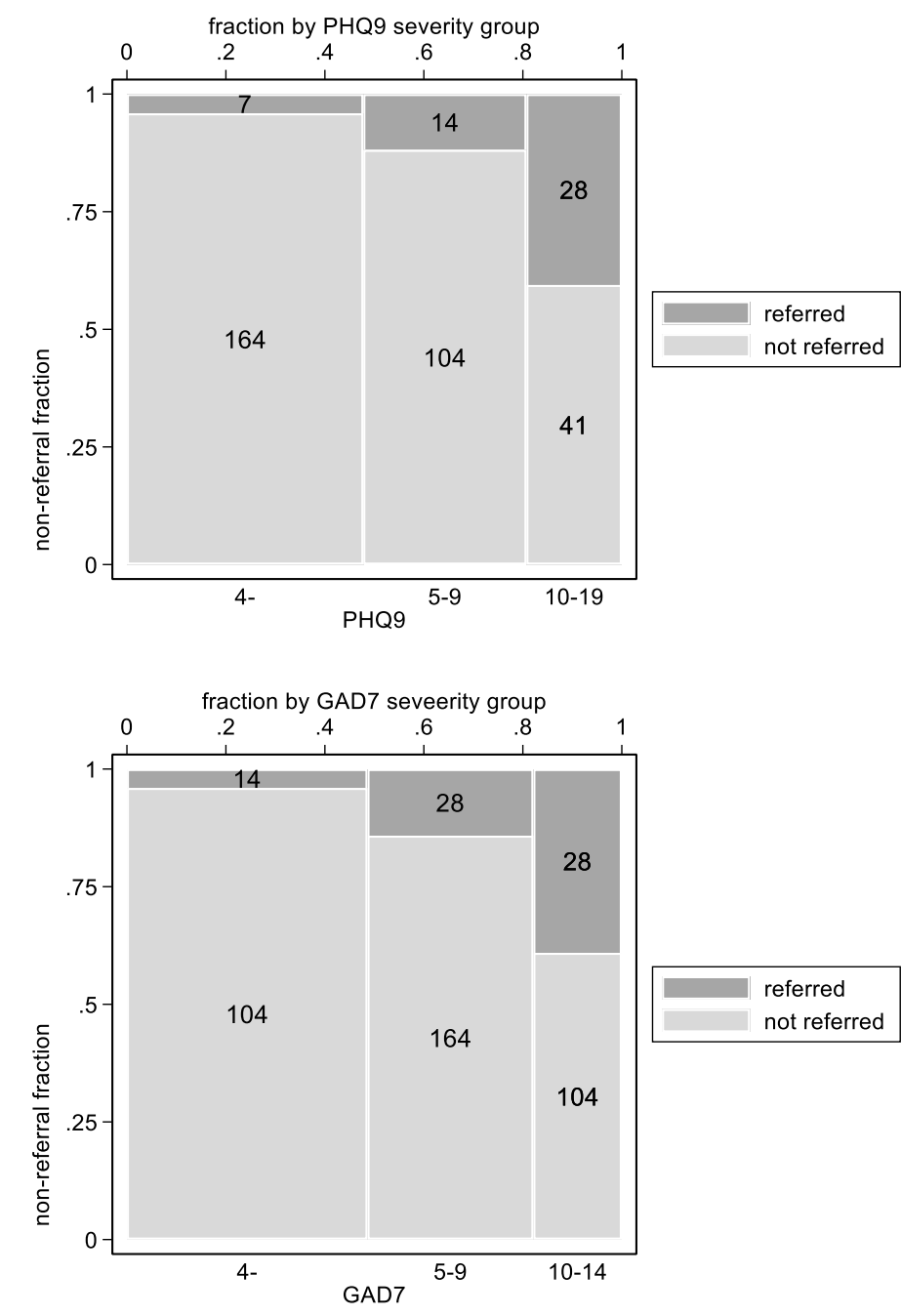
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**Supplemental Figure 1 a-b. Fraction of referral among patients in each PHQ-9 (top) and GAD-7 (bottom) severity group. The width of each vertical bar is proportional to the number of patients in the subgroup.**



Supplemental Table 1. The multivariate association of patient characteristics with PHQ-9 and GAD-7 scores

Covariate	N (%)	PHQ-9	p-value	GAD-7	p-value
Age					
30-39	21 (5.8%)	reference		reference	
40-59	85 (23.7%)	0.25 (0.10, 0.65)	0.004	0.28 (0.11, 0.72)	0.008
>60	253 (70.5%)	0.21 (0.08, 0.53)	<0.001	0.16 (0.063, 0.40)	<0.001
Female (vs Male)	174 (48.7%)	1.46 (0.97, 2.20)	0.071	1.76 (1.16, 2.67)	0.008
Education					
Elementary	46 (12.8%)	reference		reference	
Primary	130 (36.2%)	0.51 (0.28, 0.93)	0.028	0.84 (0.45, 1.57)	0.587
Secondary	130 (36.2%)	0.33 (0.18, 0.64)	0.001	0.47 (0.24, 0.91)	0.024
University	53 (14.8%)	0.14 (0.06, 0.32)	<0.001	0.47 (0.22, 1.03)	0.061

Legend Suppl Table 1 shows the association with being referred for psychological assessment. Age and sex were not associated with referral status, whereas primary vs elementary school education increased referral 5-fold, gradually reducing to a non-significant increase at university vs elementary education. Both PHQ-9 and GAD-7 scores 5-9 and  $\geq 10$  increased by about 3-4 times and 15 times, respectively the odds of referral. Multivariate models including education with either PHQ-9 or GAD-7 did not alter these estimates.