

This is a pre print version of the following article:

Non-infectious uveitis burden on quality of life and work impairment assessed through different psychometric questionnaires / Cimino, L.; Neri, P.; Miserocchi, E.; Paroli, M. P.; Vannozzi, L.; Mastropasqua, L.; Gagliano, C.; Vadala, M.; Figus, M.; Florio, F. R.; Iaccheri, B.; Mora, P.; Fossarello, M.; Balestrieri, P.; Gualberti, G.; Marando, F.; Accorinti, M.. - In: EUROPEAN JOURNAL OF OPHTHALMOLOGY. - ISSN 1724-6016. - 32:4(2022), pp. 2282-2290. [10.1177/11206721211034649]

Terms of use:

The terms and conditions for the reuse of this version of the manuscript are specified in the publishing policy. For all terms of use and more information see the publisher's website.

21/05/2024 01:13

(Article begins on next page)

Association between different psychometric questionnaires to assess the burden on quality of life and work impairment in patients with non-infectious uveitis

Luca Cimino¹, Piergiorgio Neri^{2,3}, Elisabetta Miserocchi⁴, Maria Pia Paroli⁵, Lorenzo Vannozzi⁶, Leonardo Mastropasqua⁷, Caterina Gagliano⁸, Maria Vadalà⁹, Michele Figus¹⁰, Francesca Romana Florio¹¹, Barbara Iaccheri¹², Paolo Mora¹³, Maurizio Fossarello¹⁴, Paola Balestrieri¹⁵, Giuliana Gualberti¹⁶, Francesca Marando¹⁶, and Massimo Accorinti⁵

¹Ocular Immunology Unit, Azienda USL-IRCCS, Reggio Emilia, Italy; ²Cleveland Clinic Abu Dhabi, Abu Dhabi, United Arab Emirates; ³Cleveland Clinic Lerner College of Medicine of Case Western Reserve University, Cleveland, OH, USA; ⁴Department of Ophthalmology, Vita-Salute University, San Raffaele Scientific Institute, Milan, Italy; ⁵Uveitis Center, Sapienza University of Rome, AOU Policlinico Umberto I, Rome, Italy; ⁶Department of Surgery and Translational Medicine, Eye Clinic, University of Florence, Florence, Italy; ⁷Department of Medicine and Science of Ageing, Ophthalmology Clinic, University G. d'Annunzio Chieti-Pescara, Chieti, Italy; ⁸Department of Ophthalmology, University Policlinic, Catania, Italy; ⁹Department of Biomedicine, Neuroscience and Advanced Diagnostic (BIND), Ophthalmology Section, University of Palermo, Palermo, Italy; ¹⁰Department of Surgical, Medical, Molecular Pathology and of Critical Area, University of Pisa, Pisa, Italy; ¹¹Ospedale Monospecialistico Oftalmico, UOSD Retina Medica, Roma, Italy; ¹²Department of Biomedical and Surgical Sciences, Section of Ophthalmology, University of Perugia, S. Maria della Misericordia Hospital, Perugia, Italy; ¹³Ophthalmology Unit, University Hospital of Parma, Parma, Italy; ¹⁴Clinica Oculistica, Dipartimento di Scienze Chirurgiche, Università di Cagliari, Cagliari, Italy; ¹⁵Ospedale Antonio Cardarelli, Napoli, Italy; ¹⁶Abbvie SRL, Rome, Italy.

Running title: U-quest: a novel questionnaire to assess the burden of disease in non-infectious uveitis

Word count: Abstract = 176, main text = 2940

Table/figures: 6

Corresponding Author

Luca Cimino, MD
Ocular Immunology Unit
Azienda USL-IRCCS
Reggio Emilia
Italy
Tel: +39 347/9331163
Fax: +39 0522295890
Email: cimino.luca@ausl.re.it

ABSTRACT

Background: The purpose of this study was to evaluate the association between a novel psychometric 12-item questionnaire (U-qest) and other validated questionnaires to assess quality of life and work impairment in patients with non-infectious uveitis.

Methods: Data were collected at baseline and 3 months postbaseline using U-qest and two other validated questionnaires: The National Eye Institute 25-Item Visual Function Questionnaire (VFQ-25) and the 12-Item Short-Form Health Survey (SF-12).

Results: A total of 136 patients (52.2% female) aged 47.9 ± 14.8 years (mean \pm D) were enrolled in 14 uveitis referral centres. U-qest correlated moderately with VFQ-25 and SF-12 at baseline and at 3 months. Both U-qest and VFQ-25 scores improved as disease improved; however, U-qest also detected improvement in patients for whom VFQ-25 scores did not improve. Disease activity was shown to significantly affect activity impairment. Patients and physicians expressed positive perceptions regarding the use and benefit of this instrument. U-qest showed very good reliability in terms of internal consistency (Cronbach's $\alpha=0.91$).

Conclusions: U-qest can be considered a useful tool to assess the burden of uveitis on quality of life.

KEYWORDS: Uveitis, questionnaire, QoL, disease burden, work impairment

INTRODUCTION

Uveitis represents a heterogeneous group of diseases affecting different portions of the uveal tract and other ocular tissues¹. It most frequently occurs in adults aged 20 to 50 years², affecting their quality of life (QoL) and carrying a social and economic burden². The QoL of patients with uveitis is affected not only by their visual impairment but also by associated systemic diseases and treatment-related side effects³. Mental disorders have also been observed in patients affected by uveitis, negatively influencing work ability, study performance, and career progression^{3,4}.

Questionnaires have been developed to help measure health-related QoL in patients with vision-related disease, such as the National Eye Institute 25-Item Visual Function Questionnaire (VFQ-25)⁵ and Visual Function Questionnaire Utility Index¹. Both questionnaires evaluate patient perception on vision performance and provide a validated analysis of the data collected. However, the structure of these questionnaires is complex and could be problematic for patients with severe vision disability³.

The Medical Outcomes Study 36-Item Short Form Health Survey (SF-36)^{6,7}, another validated questionnaire, was developed to provide 8 dimensions. The 12-Item Short Form Health Survey (SF-12) is a shorter alternative to the SF-36⁸.

However, no studies on QoL and work productivity in patients affected by uveitis have been conducted in Italy thus far, perhaps owing to a lack of an appropriate QoL questionnaire. The aim of this study was to assess a new user-friendly e-questionnaire—U-quest—measuring QoL in patients affected by chronic or recurrent non-infectious uveitis.

METHODS

Patients and study design

This prospective, multicentre, longitudinal, observational study compared the U-quest to the VFQ-25 and SF-12 in patients affected by chronic or recurrent non-infectious uveitis. It was conducted in 14 centres across Italy (**Supplementary Material Table 1**), with data collected at baseline, 2 to 7 days postbaseline (visit 2), and at 3 months postbaseline (visit 3).

Inclusion criteria were age ≥ 18 years, a diagnosis of chronic or recurrent non-infectious uveitis, and the ability to understand and complete questionnaires. Patients excluded from the study were those affected by Fuchs uveitis, malignancies, human immunodeficiency virus, or severe psychiatric comorbidities and those participating in other clinical trials on uveitis. The Standardization of Uveitis Nomenclature International Working Group⁹ criteria were used to assess uveitis status. Written informed consent was obtained from all patients and submitted to the local ethics committee in accordance with the Declaration of Helsinki.

U-quest design and structure

The U-quest study was conducted in Italy from July through November 2016. Five Italian members of the International Uveitis Study Group designed the questionnaire to address the following 12 areas (**Supplementary Material Table 2**): general state of body self-perception, self-sufficiency, daily activities, work, psychological self-perception, mood, anxiety, personal relationships, social self-perception, future family plans, romantic relationships, and social life. The questionnaire, written in Italian, was uploaded onto an electronic platform developed in accordance with the US Food and Drug Administration PRO Guidance for Industry¹⁰. Patients completed the U-quest in the presence of a designated physician at

baseline and at the two follow-up visits. Patients were asked to rank their answers using a visual analogue scale, with responses ranging from 0 (“absolutely not”) to 10 (“definitely yes”). A smartphone application allowed patients to change the contrast and the size of the characters, read the questions aloud, confirm the chosen score, and see a visual representation of the total score. Audio support was also included with this application. A graphical output was produced by linking the scores of the questions, facilitating comparison between visits (**Supplementary Material Figure 1**). The final score was the sum of the scores of all 12 questions, from 0 (no effect of the disease on QoL) to 120 (maximum effect of disease on QoL).

VFQ-25, SF-12, and WPAI questionnaires

The QoL questionnaires VFQ-25⁵ and SF-12⁸ as well as the Work Productivity and Activity Impairment (WPAI)¹¹ questionnaire were used as control tests to validate U-quest at baseline and the two follow-up visits.

Psychometric evaluation

Psychometric evaluation was performed at different time points. Data collected at the first visit (baseline) were used to test the internal consistency and construct validity of the instrument; data collected at visit 2 were used to test the reliability of the instrument; data collected at 3 months (depending on routine visit schedules) were used to test the U-quest responsiveness to change.

Construct validity

To assess construct validity, the correlation of U-quest score versus VFQ-25 and SF-12 were analysed clinically and psychometrically at baseline. Differences in scores regarding severity

of uveitis and QoL as measured by the VFQ-25 and SF-12 were examined, hypothesizing that patients reporting higher levels of severity and lower QoL in those questionnaires should have higher U-quest scores.

Responsiveness

Responsiveness was tested using the paired *t* test to compare the change in scores between two groups of patients between the first and last visit. Statistical significance was assessed both within groups (i.e., change in score among patients rating themselves as improved) and between groups (i.e. change in score among patients rating themselves as improved vs not improved). The change in clinical condition was tested in two different ways: based on the severity (active to inactive disease, according to physician's clinical evaluation) and based on the changes in activity of the disease, as perceived by the patient. Answers regarding patient satisfaction and perception ("According to you today the seriousness of your uveitis is...") were categorized into 3 classes ("very mild or mild"/"fair"/"high or very high") and patients rated as not improved or worsened are those whose perception of their severity of illness did not change or changed for the worse.

Statistical analysis

Test-retest reliability was estimated by administering the same questionnaire to the same patients at visit 2. The Pearson's correlation coefficient between the two sets of responses was used as a quantitative measure of the test-retest reliability.

Internal consistency reliability was determined using Cronbach's coefficient alpha to calculate the pairwise correlations between items. Internal consistency ranges from 0 to 1. A commonly accepted rule of thumb is that an alpha of 0.6 to 0.7 indicates acceptable

reliability and ≥ 0.8 indicates good reliability.

Sample size was determined according to feasibility criteria as previously described¹².

According to these criteria, 10 subjects per questionnaire item were needed. The U-qest questionnaire comprises 12 items and, therefore, a minimum of 120 subjects was required.

Data are presented using mean, standard deviation, median, and range. Categorical variables are summarized by using frequency distribution and percentages. A p value of ≤ 0.05 was considered statistically significant. Statistical analyses were performed using Stata 13.0 (StataCorp LLC, College Station, TX, USA).

RESULTS

Patient baseline demographic characteristics

A total of 136 patients were enrolled across 14 ophthalmology hospital/university centres. The mean \pm SD age was 47.9 \pm 14.8 years, and 52.2% were female (**Table 1**). Most patients (n=89 [65%]) had at least a high school degree, and most (n=83 [61%]) were married or living with a partner. Fifty-five patients (40.4%) had \geq 1 comorbid disease, the most frequent being hypertension (n=31 [22.8%]), and 51 (37.5%) were receiving systemic corticosteroids. Other treatments for uveitis included systemic conventional immunosuppressive drugs, such as azathioprine (n=13 [9.6%]), cyclosporin A (n=15 [11%]), mycophenolate mofetil (n=6 [4.4%]) or methotrexate (n=15 [11%]). Thirty (22.1%) patients were being treated with biological drugs.

Uveitis disease characteristics

Disease characteristics of patients with uveitis at study entry are summarised in **Table 2** and **Table 3**. Median (interquartile range) time from first symptoms of uveitis was 67 (32–123) months, and time from diagnosis was 55 (24–116) months. The majority of patients (n=89 [65.4%]) had uveitis in both eyes. Most patients had anterior uveitis (n=51 [37.5%]) and panuveitis (n=44 [32.4%]). The main cause of uveitis was idiopathic (n=41 [30.2%]) or Behçet disease (n=20 [14.7%]). One-third of patients had active uveitis (n=45 [33.1%]).

U-qest, VFQ-25, SF-12, and WPAI-uveitis questionnaires

Although a slight reduction (improvement) in mean U-qest score versus baseline was observed in patients after 3 months, scores for other questionnaires remained largely unchanged between the two visits (**Figure 1A**). Stratifying patients by active versus inactive

disease showed a similar trend among the different questionnaires at baseline and the 3-month visit (**Figure 1B** and **1C**). At baseline, scores indicating a worse QoL were observed in patients with active versus inactive disease for U-qest, VFQ-25, and SF-12 Mental Component Summary (MCS; **Figure 1B**), and, although this trend was maintained at 3 months, only the VFQ-25 questionnaire detected a significant difference between groups (**Figure 1C**).

The effect of uveitis on a patient's ability to work and productivity was also assessed in patients with active versus inactive disease using the WPAI uveitis score (**Figure 2**). No difference was observed among the 4 measures (absenteeism, presenteeism, work impairment, or activity impairment) between baseline and the 3-month visit (**Figure 2A**), whereas when stratifying patients by disease activity (inactive vs active disease), statistically significant differences in the burden of active disease on work-related measures (with the exception of absenteeism) were observed at both baseline (**Figure 2B**) and 3 months (**Figure 2C**).

When patients were stratified by the presence or absence of underlying systemic diseases, we observed that the SF-12 Physical Component Summary (PCS) was significantly worse (i.e., lower) at 3 months for those with (46 ± 8.7) versus without (50.98 ± 6.3) systemic disease ($p < 0.001$). No differences were observed at 3 months for the other questionnaires.

When patients were stratified according to anatomic classification, a similar trend was observed in the U-qest and VFQ-25 questionnaires at baseline (**Supplementary Material Figure 2A**) and 3 months (**Supplementary Material Figure 2B**): patients with intermediate uveitis reported less severe disease compared with those with panuveitis, who reported a

higher burden of disease (**Supplementary Material Figure 2A and 2B**). No difference based on anatomical classification was observed at baseline or 3 months according to SF-12 MCS or PCS.

Patient and physician perception of U-qest questionnaire

Patient perception of the U-qest questionnaire was assessed through four specific questions (**Table 4**). Approximately 70% of patients reported that the severity of their uveitis was between “fair” and “very high” (question 1), and approximately 90% of patients reported overall positive perception (“moderately”, “quite a lot”, and “very much”) when assessing this instrument (questions 2 and 3) and its role in improving their relationship with their ophthalmologist (question 4). No discernible difference was observed in patient perception of the questionnaire from baseline to the 3-month visit (**Table 4**). Physician perception of the U-qest was also very positive and higher than patient perceptions; 61.54% of physicians reported that they were “very much” satisfied with the questionnaire, and an increased percentage of physicians (from 38.46% at baseline to 53.85% at 3 months) reported being “very much” satisfied with this questionnaire for providing them with a better understanding of the problems experienced by their patients owing to uveitis.

Construct validity

The grade of correlation of the U-qest score with the VFQ-25 was moderate (-0.60 [95% CI, -0.72 to -0.49]). The grade of correlation of the U-qest score with the SF-12 was low for PCS (-0.37 [95% CI, -0.52 to -0.23]) and moderate for MCS (-0.55 [95% CI, -0.67 to -0.43]).

Internal consistency and stability

The overall reliability of the U-quest questionnaire was very good for both internal consistency (Cronbach's alpha, 0.91) and stability: according to test-retest, the Pearson correlation with baseline for the second visit was 0.75 (95% CI, 0.61 to 0.89).

Responsiveness

The change in questionnaire scores (in terms of activity and severity of disease) from baseline to 3 months was evaluated from the perspective of the physician and patient (**Supplementary Material Table 3**). After 3 months, patients who improved and patients who did not improve or who remained unchanged (according to their physicians) showed a significant decrease in U-quest score compared with baseline; U-quest reports a statistically significant improvement in QoL, although to a different extent. There was no significant difference between patients who improved, and those who did not improve or remained unchanged.

Regarding VFQ-25, patients who improved, on average, showed a score increase, although it was not statistically significant. Patients who did not improve or worsened had a significant mean score decrease, therefore VFQ-25 scores moved in the expected direction. When comparing these mean changes between groups we observed a significant difference.

For SF-12 PCS and MCS, both groups of patients reported no change, on average, and no significant difference between groups was observed. When this analysis was repeated to evaluate U-quest score according to question 1 of the patients' perception of the severity of illness (activity of disease), results were similar to those observed for physicians' perception.

DISCUSSION

Current literature on the effect of chronic or recurrent non-infectious uveitis on QoL in the Italian population is largely limited, with no studies available on its effect on work impairment or productivity. Two Italian studies were previously conducted^{6,13}, but both were single-centre studies and both used the SF-36 questionnaire, which does not collect information on all the areas of well-being and functioning that may be of importance to patients with uveitis. These studies^{6,13} and others not performed in Italy^{14–16} have consistently shown that QoL is significantly affected in patients with non-infectious uveitis compared with health individuals.

To address this unmet need, the U-qest questionnaire was developed to explore 12 general areas reflecting QoL. In fact, whereas the VFQ-25 evaluates vision-specific aspects and the SF-12 is a generic measure of health-related QoL, U-qest was designed as a generic measure of those aspects of QoL specifically affected by uveitis.

Several important findings have emerged from the present study. We observed a moderate correlation between U-qest scores and VFQ-25 and SF-12 questionnaire scores at baseline.

In patients with an improvement in disease, both U-qest and VFQ-25 scores improved, however, U-qest also detected a significant improvement in patients for whom VFQ-25 scores reported stable or worsening disease. This may be attributed to the low sample size, other comorbid diseases in this subgroup, or heterogeneity of the aetiology and the variability of the clinical picture of uveitis. It is also possible that the study's duration was insufficient to detect a measurable improvement, or that the patient's positive reaction to the attention paid by ophthalmologists to their QoL and well-being affected their scores.

Furthermore, we observed that work and productivity impairment were significantly

affected in patients with active versus inactive disease using the WPAI uveitis questionnaire, confirming previous findings¹⁷.

Recent evidence from a study conducted in Spain showed that lower best corrected visual acuity and the presence of ocular comorbidities were negatively associated with vision-related QoL in patients with non-infectious uveitis¹⁸. A study performed in Australia demonstrated that patients with uveitis had significantly poorer vision-related and health-related QoL compared with healthy individuals¹⁹. Although we did not observe any discernible differences in scores for patients with versus without ocular comorbidities among the different questionnaires (possibly because of the limited number of patients available), we did observe a significant worsening at 3 months in SF-12 PCS scores from baseline in patients with versus without systemic diseases.

No difference in questionnaire scores by classification of uveitis was observed, although we did observe a trend in which patients with posterior uveitis or panuveitis had more severe disease compared with anterior uveitis. This trend was seen in U-qest and VFQ-25 questionnaires only and corroborates with findings by Schiffman et al¹⁴, but not with findings by Fabiani et al, in which a more severe effect on QoL in patients with acute anterior uveitis compared with those with panuveitis was found¹³.

Panuveitis is treated with systemic (e.g., corticosteroids and biologic agents) and topical therapies whereas anterior uveitis is usually managed with topical therapies only.

Differences in underlying severity among patient cohorts as well as their therapeutic management may account for the differences observed across studies^{13,14}.

Finally, we also evaluated the patient and physician perception of the questionnaire and observed favourable responses (>70% positive response). This feature of the questionnaire highlights the importance of the psychological burden of uveitis, often reflected in poor scores in the MCS in the SF-12 and SF-36 questionnaires¹⁴⁻¹⁶, but not in all studies¹³.

Although an assessment of clinical severity is always performed, the effect of non-infectious uveitis on the patient QoL is rarely performed outside specialized centres. Hence, patients are seldom asked to discuss the outcome of the tests in subsequent interviews. However, there is evidence that incorporating an instrument to assess the effect of a disease on the patient's QoL into the routine medical practice can induce greater patient satisfaction, improved compliance, and even improve clinical outcome²⁰.

The mean \pm SD age of patients who participated the present study (47.9 \pm 14.9 years) was similar to other studies²¹⁻²⁴, highlighting that the visual impairment secondary to uveitis usually affects an adult population of working age, imposing changes in QoL with significant social and economic impact. The assessment of disease severity and QoL in patients with non-infectious uveitis is not sufficiently performed in daily practice. This is mainly due to the lack of fast and visually sensitive instruments and intuitive tools, particularly regarding QoL. Our tool is meant to be administered through a smartphone application, which would allow both physician and patient to have an immediate representation of the progress achieved. Having a global picture of the patient's status can help the clinician make decisions regarding therapy, even when uveitis is under control but the perceived burden of the current treatment is destabilizing for the patient.

Conclusion

Evaluating changes in QoL associated with the clinical course of disease is essential to improve the management of non-infectious uveitis. U-qest can be considered a useful tool for a global assessment of the effect of uveitis on QoL. This psychometric questionnaire provides an additional, disease-specific, useful, self-administered instrument that measures QoL, helping to develop a good patient-physician relationship. Future studies will aid in our understanding of the effect of non-infectious uveitis on QoL in relation to clinical course.

ACKNOWLEDGEMENTS

Medical writing support and editorial assistance was provided by Colin Gerard Egan, PhD (CE Medical Writing, Pisa, Italy), and was funded by AbbVie (no grant number).

The authors thank Cesare Mariotti (Department of Ophthalmology, University of Ancona, Ancona, Italy) for his help in recruiting the patients and Claudia Cornacchia of AbbVie, for U-quest realization and study implementation and management.

AUTHOR CONTRIBUTIONS

Luca Cimino, Piergiorgio Neri, Elisabetta Miserocchi, Maria Pia Paroli, Giuliana Gualberti and Massimo Accorinti contributed to the U-quest ideation and development and to protocol ideation. Francesca Marando, Giuliana Gualberti and Massimo Accorinti contributed to data analysis and interpretation of results.

Luca Cimino, Elisabetta Miserocchi, Maria Pia Paroli, Lorenzo Vannozzi, Leonardo Mastropasqua, Caterina Gagliano, Maria Vadalà, Michele Figus, Francesca Romana Florio, Barbara Iaccheri, Paolo Mora, Maurizio Fossarello, Paola Balestrieri, and Massimo Accorinti enrolled patients and collected study data.

All authors equally contributed to the writing and reviewing of the manuscript and approved the final version.

DECLARATION OF CONFLICTING INTERESTS

G Gualberti and F Marando are AbbVie employees and may own AbbVie stocks and options.

L Cimino received consultancy fees from AbbVie and Santen. All other authors have no conflict of interest to declare.

FUNDING

The author(s) disclosed receipt of the following financial support for the research, authorship, and/or publication of this article: AbbVie Srl (Rome, Italy) sponsored this study and editorial assistance for the writing of the manuscript. AbbVie participated in the study design, interpretation of data, and writing of the publication.

REFERENCES

1. Naik RK, Gries KS, Rentz AM, Kowalski JW, Revicki DA. Psychometric evaluation of the National Eye Institute Visual Function Questionnaire and Visual Function Questionnaire Utility Index in patients with non-infectious intermediate and posterior uveitis. *Qual Life Res Int J Qual Life Asp Treat Care Rehabil*. 2013;22(10):2801-2808. doi:10.1007/s11136-013-0412-y
2. Durrani OM, Tehrani NN, Marr JE, Moradi P, Stavrou P, Murray PI. Degree, duration, and causes of visual loss in uveitis. *Br J Ophthalmol*. 2004;88(9):1159-1162. doi:10.1136/bjo.2003.037226
3. de Smet MD, Taylor SRJ, Bodaghi B, et al. Understanding uveitis: the impact of research on visual outcomes. *Prog Retin Eye Res*. 2011;30(6):452-470. doi:10.1016/j.preteyeres.2011.06.005
4. Onal S, Oray M, Yasa C, et al. Screening for Depression and Anxiety in Patients with Active Uveitis. *Ocul Immunol Inflamm*. 2018;26(7):1078-1093. doi:10.1080/09273948.2017.1319959
5. Rentz AM, Kowalski JW, Walt JG, et al. Development of a preference-based index from the National Eye Institute Visual Function Questionnaire-25. *JAMA Ophthalmol*. 2014;132(3):310-318. doi:10.1001/jamaophthalmol.2013.7639
6. Miserochi E, Modorati G, Mosconi P, Colucci A, Bandello F. Quality of life in patients with uveitis on chronic systemic immunosuppressive treatment. *Ocul Immunol Inflamm*. 2010;18(4):297-304. doi:10.3109/09273941003637510
7. Patrick DL, Deyo RA. Generic and disease-specific measures in assessing health status and quality of life. *Med Care*. 1989;27(3 Suppl):S217-232.
8. Ware J, Kosinski M, Keller SD. A 12-Item Short-Form Health Survey: construction of scales and preliminary tests of reliability and validity. *Med Care*. 1996;34(3):220-233.
9. Jabs DA, Nussenblatt RB, Rosenbaum JT, Standardization of Uveitis Nomenclature (SUN) Working Group. Standardization of uveitis nomenclature for reporting clinical data. Results of the First International Workshop. *Am J Ophthalmol*. 2005;140(3):509-516.
10. Food and Drug Administration Guidance for Industry. Patient-Reported Outcome Measures: Use in Medical Product Development to Support Labeling Claims. Published online 2009. <https://www.fda.gov/regulatory-information/search-fda-guidance-documents/patient-reported-outcome-measures-use-medical-product-development-support-labeling-claims>
11. Reilly MC, Gooch KL, Wong RL, Kupper H, van der Heijde D. Validity, reliability and responsiveness of the Work Productivity and Activity Impairment Questionnaire in

- ankylosing spondylitis. *Rheumatol Oxf Engl*. 2010;49(4):812-819. doi:10.1093/rheumatology/kep457
12. Streiner DL, Norman GR, Cairney J. *Health Measurement Scales: A Practical Guide to Their Development and Use*. Fifth Edition. Oxford University Press; 2014.
 13. Fabiani C, Vitale A, Orlando I, et al. Impact of Uveitis on Quality of Life: A Prospective Study from a Tertiary Referral Rheumatology-Ophthalmology Collaborative Uveitis Center in Italy. *Isr Med Assoc J IMAJ*. 2017;19(8):478-483.
 14. Schiffman RM, Jacobsen G, Whitcup SM. Visual functioning and general health status in patients with uveitis. *Arch Ophthalmol Chic Ill 1960*. 2001;119(6):841-849.
 15. Hui MM, Wakefield D, Patel I, Cvejic E, McCluskey PJ, Chang JH. Visual Functioning and Health-related Quality-of-Life are Compromised in Patients with Uveitis. *Ocul Immunol Inflamm*. 2017;25(4):486-491. doi:10.3109/09273948.2016.1139734
 16. Maca SM, Wagner J, Weingessel B, Vécsei-Marlovits PV, Gruber K, Schiesser AW. Acute anterior uveitis is associated with depression and reduction of general health. *Br J Ophthalmol*. 2013;97(3):333-337. doi:10.1136/bjophthalmol-2012-302304
 17. Jalil A, Yin K, Coyle L, Harper R, Jones NP. Vision-related quality of life and employment status in patients with uveitis of working age: a prospective study. *Ocul Immunol Inflamm*. 2012;20(4):262-265. doi:10.3109/09273948.2012.684420
 18. Arriola-Villalobos P, Abásolo L, García-Feijoo J, et al. Vision-related Quality of Life in Patients with Non-infectious Uveitis: A Cross-sectional Study. *Ocul Immunol Inflamm*. 2018;26(5):717-725. doi:10.1080/09273948.2017.1285034
 19. Hui MM, Wakefield D, Patel I, Cvejic E, McCluskey PJ, Chang JH. Visual Functioning and Health-related Quality-of-Life are Compromised in Patients with Uveitis. *Ocul Immunol Inflamm*. 2017;25(4):486-491. doi:10.3109/09273948.2016.1139734
 20. Linder D, Sampogna F, Torreggiani A, et al. Psodisk, a new visual method for assessing the burden of psoriasis on patients. *J Eur Acad Dermatol Venereol JEADV*. 2012;26(9):1163-1166. doi:10.1111/j.1468-3083.2011.04192.x
 21. Rothova A, Suttorp-van Schulten MS, Frits Treffers W, Kijlstra A. Causes and frequency of blindness in patients with intraocular inflammatory disease. *Br J Ophthalmol*. 1996;80(4):332-336.
 22. Durrani OM, Meads CA, Murray PI. Uveitis: a potentially blinding disease. *Ophthalmol J Int Ophthalmol Int J Ophthalmol Z Augenheilkd*. 2004;218(4):223-236. doi:10.1159/000078612
 23. Schiffman RM, Jacobsen G, Whitcup SM. Visual functioning and general health status in patients with uveitis. *Arch Ophthalmol Chic Ill 1960*. 2001;119(6):841-849.

24. Frick KD, Drye LT, Kempen JH, et al. Associations among visual acuity and vision- and health-related quality of life among patients in the multicenter uveitis steroid treatment trial. *Invest Ophthalmol Vis Sci.* 2012;53(3):1169-1176. doi:10.1167/iovs.11-8259

Figure legends

Figure 1. U-quest, VFQ-25 and SF-12 questionnaires scores. Scores are presented as mean \pm SD, and p values represent statistically significant differences between active and inactive disease groups based on all patients (N=136). **(A)** Baseline and 3 month values; **(B)** baseline active vs inactive values; **(C)** 3-month active vs inactive values. The VFQ-25 is composed of 25 items and was developed to assess the influence of visual impairment and visual symptoms in general health⁵. It is used to assess the QoL in individuals with chronic eye diseases through 12 domains, 1 related to general health and 11 specifically related to vision. All subscale scores range from 0–100, with 100 representing maximum visual function. The SF-12 consists of 12 questions covering eight domains to measure health, including physical and mental components of QoL⁸. The analysis of these areas results in two summary measures: Physical Component Summary (PCS) and the Mental Component Summary (MCS). Subscale scores range from 0%–100%, with higher scores indicating better health. VFQ-25 = 25-Item Visual Function Questionnaire; SF-12 = 12-Item Short Form Health Survey; MCS = Mental Component Summary; PCS = Physical Component Summary.

Figure 2. Effect of uveitis on the ability to work and on productivity using the WPAI uveitis questionnaire. Scores are presented as mean \pm SD, and p values represent statistically significant differences between active and inactive disease groups. **(A)** Baseline and 3-month values; **(B)** baseline active vs inactive values; **(C)** 3-month active vs inactive values. The WPAI questionnaire was used to measure the effect of overall health and specific symptoms on productivity at work and outside work¹¹. It consists of six items evaluating four domains: (1) activity impairment (percentage impairment in daily activities), (2) overall work productivity

loss, (3) presenteeism (percentage of impairment experienced at work owing to health problems) and (4) absenteeism (percentage of working time missed owing to health problems). Higher scores indicate a greater degree of work productivity loss and activity impairment. ABS = absenteeism; ACT IMP = activity impairment; PRES = presenteeism, WK IMP = work impairment; WPAI = Work Productivity and Activity Impairment.