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Improvements in vision-related quality of life in blind patients implanted with the Argus II Epiretinal Prosthesis

Background: The purpose of this analysis is to report the change in quality of life (QoL) after treatment with the Argus II Epiretinal Prosthesis in patients with end-stage retinitis pigmentosa.

Methods: The Vision and Quality of Life Index (VisQoL) was used to assess changes in QoL dimensions and overall utility score in a prospective 30-patient single-arm clinical study. VisQoL is a multi-attribute instrument consisting of six dimensions (injury, life, roles, assistance, activity, and friendship) that may be affected by visual impairment. Within each dimension, patients were divided into two groups based on how much their QoL was affected by their blindness at baseline (moderate/severe or minimal). Outcomes were compared within each dimension subgroup between baseline and the combined follow-up periods using the Friedman test. In addition, data from the six dimensions were combined into a single utility score, with baseline data compared to the combined follow-up periods.

Results: Overall, 80 per cent of the patients reported difficulty in one or more dimensions pre-implant. Composite VisQoL utility scores at follow-up showed no statistically significant change from baseline; however, in three of the six VisQoL dimensions (injury, life, and roles), patients with baseline deficits showed significant and lasting improvement after implantation with Argus II. In two of the three remaining dimensions (assistance and activity), data trended toward an improvement. In the final VisQoL dimension (friendship), none of the patients reported baseline deficits, suggesting that patients had largely adjusted to this attribute.

Conclusion: Patients whose vision negatively affected them with respect to three VisQoL dimensions (that is, getting injured, coping with the demands of their life and fulfilling their life roles) reported significant improvement in QoL after implantation of the Argus II retinal prosthesis. Furthermore, the benefit did not deteriorate at any point during the 36-month follow-up, suggesting a long-term, durable improvement.
to slow the rate of retinal degeneration, although there is no evidence that it halts photoreceptor degeneration. Other therapeutic modalities under development include gene therapy, stem cell transplantation and pharmacologic options to preserve the remaining photoreceptors. At present, a retinal prosthetic device is the only therapy commercially available to treat patients with advanced RP.

The Argus II Retinal Prosthesis System (Second Sight Medical Products, Inc, Sylmar, California, USA) was approved by the Food and Drug Administration (FDA) in 2013 for treatment of late-stage RP. The device includes a small video camera that is built into a special pair of eyeglasses. The camera is connected to a video processing unit worn by the patient, which converts the video input to electronic signals that are transmitted wirelessly to an electrode array (60 electrodes arranged in a six by ten grid) implanted on the surface of the retina. The array stimulates remaining ganglion and/or bipolar cells in the retina and this activation pattern is then transmitted by the optic nerve to the brain, where it is perceived as patterns of light. The patient learns to interpret these patterns so he or she can distinguish the movement and outlines of objects.

The safety and benefit of Argus II were established in a prospective 30-patient single-arm clinical study.5,6 Patients participating in the study had baseline visual acuity of worse than 2.9 logMAR in both eyes (worse than 6/4,764 in Snellen notation), as measure with a grading visual acuity test and the device was implanted in the worse-seeing eye. Efficacy was established from three computer-based, objective tests of basic visual skills, intended to measure incremental changes in a low-vision population. Functional vision or the ability to complete everyday tasks, was also measured with the device turned on and off.7

In addition to objective and observer-rated outcome measures, the FDA advises using a patient-reported outcome measure, such as a quality of life (QoL) instrument, when the concept being measured is best known by the patient or best measured from the patient’s perspective.7 QoL is an important aspect of treatment efficacy; it is reported that QoL is reduced in patients with RP compared to normal controls.8 However, it has also been reported that patients with RP may adapt to progressive loss of vision, resulting in a minimal decrease in self-reported QoL, particularly within certain dimensions.9 To the authors’ knowledge, there are no published reports on the change in QoL in patients implanted with a retinal prosthesis.

To evaluate the effect of some restoration of vision on RP patients’ QoL, QoL was measured in the Argus II clinical trial with a vision-specific multi-attribute utility instrument developed by researchers at The University of Melbourne (East Melbourne, Victoria, Australia) and Monash University (Clayton, Victoria, Australia). The Vision and Quality of Life Index (VisQoL) differs from generic QoL instruments insofar as it attempts to be more responsive to clinically relevant changes in vision.

This analysis is the first published report on VisQoL changes in patients with RP implanted with the Argus II retinal prosthesis. It also represents one of the first attempts to measure changes in QoL in a population with profound loss of vision and who receive a sight restoration intervention. Finally, this analysis identifies which VisQoL dimensions are most influenced by end-stage RP and which QoL subscales are most affected by implantation of a retinal prosthesis.

METHODS

Study design and patients
Thirty patients were enrolled in a single-arm, prospective, unmasked clinical trial conducted at 10 centres in the USA and Europe. The study size was necessarily limited to the patient population with profound loss of vision as found in the Argus II cohort.

The VisQoL survey was administered to all patients implanted in the Argus II cohort. Vision-specific QoL was measured using the VisQoL multi-attribute utility instrument. VisQoL covers six dimensions (or attributes) of QoL as detailed in Table 2. Survey options are registered on a five- or six-point scale. A utility score for each dimension is estimated, based on participant surveys using the time trade-off method.12 All six dimensions are combined using a multiplicative model resulting in a utility score ranging from zero to one (where zero represents death and one represents full health). Although the instrument has been validated for a low-vision population, it has not been validated for patients with RP or patients with severe loss of vision as found in the Argus II cohort.

The VisQoL survey was administered to all 30 patients at baseline. One patient was explanted at 14 months and thus was withdrawn from the study and from the analysis. Follow-up visits were completed at three, six, 12, 18, 24 and 36 months. Device outcomes were considered stable beginning with the 12-month follow-up visit.

Table 1. Demographic data from the Argus II clinical trial
Table 2. Vision and Quality of Life Index (VisQoL) dimensions with scoring scale. Within each dimension, lower scores reflect little to no effect on quality of life caused by loss of vision. Scores shown in bold represent worse outcomes associated with the visual loss. All six dimensions are combined to form a single utility score ranging 0-1. Each dimension is identified by the term underlined (for example, dimension 1 is referred to as ‘injury’ dimension).

1. Does my vision make it likely I will injure myself (that is, when moving around the house, yard, neighbourhood or workplace)?
   - 1 = Unlikely
   - 2 = Small chance
   - 3 = Good chance
   - 4 = Very likely
   - 5 = Almost certainly

2. Does my vision make it difficult to cope with the demands in my life?
   - 1 = No effect
   - 2 = Not difficult
   - 3 = Little difficulty
   - 4 = Moderately difficult
   - 5 = Very difficult
   - 6 = Unable

3. Does my vision affect my ability to have friendships?
   - 1 = Not difficult
   - 2 = Little difficulty
   - 3 = Moderately difficult
   - 4 = Lot of difficulty
   - 5 = Unable

4. Do I have difficulty organising any assistance I may need?
   - 1 = No effect
   - 2 = Not difficult
   - 3 = Little difficulty
   - 4 = More difficult
   - 5 = Extremely difficult
   - 6 = Unable

5. Does my vision make it difficult to fulfil the roles I would like to fulfil in my life (for example, family roles, work roles, community roles)?
   - 1 = No effect
   - 2 = Not difficult
   - 3 = Little difficulty
   - 4 = Moderately difficult
   - 5 = Very difficult
   - 6 = Unable

6. Does my vision affect my confidence to join in everyday activities?
   - 1 = More confident
   - 2 = No effect
   - 3 = Little less confident
   - 4 = Moderately less confident
   - 5 = Lot less confident
   - 6 = Not confident

Statistical analysis

Computations were carried out using SAS 9.4 (SAS Inc., Cary, North Carolina, USA).

Data from the VisQoL questionnaire were converted to a single utility score (ranging between zero to one) using the scoring algorithm provided by the Assessment of Quality of Life group. The resulting baseline scores were analysed with descriptive statistics and analysis of variance (ANOVA) was used to compare baseline data with that generated at 12, 18, 24 and 36 months.

A further analysis was done within each of the six VisQoL dimensions. For this analysis, patients who perceived little or no effect of their loss of vision on QoL were considered separately from those whose blindness was affecting their QoL at baseline with scores shown in bold in Table 2. Outcomes (mean survey scores) were compared within each sub-group between baseline and the combined follow-up periods (12 to 36 months) using the Friedman test (that is, a longitudinal analysis was completed using repeated measurements and a non-parametric test method).

In spite of limited demographic data, univariate and multivariate tree analysis with baseline utility scores were completed. Pearson correlations with age and years with RP are reported. The t-test was used to analyse outcomes by gender. Multivariate regression tree analysis was completed on four groups defined by age, gender and years with RP.

RESULTS

Overall baseline (pre-implant) utility scores from analysis of all six VisQoL dimensions are detailed in Figure 1. Within the 30-patient cohort, baseline utility scores ranged 0.22-0.99 (normal distribution) even though all patients had significant visual loss (worse than 2.9 logMAR).

VisQoL utility scores at follow-up (post-implant) showed no statistically significant change from baseline. Mean utility scores ranged between 0.63 to 0.67 throughout the follow-up period (versus 0.62 at baseline).

Because of the large distribution of baseline utility scores, patients within each of the six VisQoL dimensions were sub-divided into those who reported minimal difficulty in performing any given dimension at baseline in spite of loss of vision and those who reported having at least moderate difficulty (Table 2, which identifies in bold text the responses representing at least moderate difficulty). Outcomes (change in survey scores) for five of the six VisQoL dimensions within the sub-group of patients whose blindness was affecting their QoL at baseline are provided in Table 3. One VisQoL dimension (Friendship – item 3 in Table 2) had no patients who reported difficulty caused by their visual loss at baseline and therefore, was not analysed. Although the data are not normally...
Within each VisQoL dimension, between nine and 20 patients (30 to 67 per cent) reported at least moderate impact of their visual loss on their QoL. The remaining patients self-reported minimal difficulty in performing any given dimension at baseline. Overall, 80 per cent of the cohort reported a significant impact of their vision on QoL at baseline in at least one of the five affected dimensions, confirming that the majority of patients had baseline QoL deficits.

In three dimensions (injury, life and roles), those whose QoL was affected by their loss of vision had significant improvement in the follow-up phase of the study (that is, survey scores decreased in value). For these three dimensions, at least 50 per cent of the subjects reported their vision negatively affected their QoL with respect to the dimension. Furthermore, those whose QoL was not affected by their loss of vision within the same three dimensions had no significant change from baseline at follow-up.

In the other two dimensions (assistance and activity), data trended toward an improvement in QoL, although there was insufficient power to demonstrate significance (less than one-third of the study cohort reported difficulty at baseline in either dimension).

The improvements in VisQoL scores within the subgroup of subjects who reported an impact of blindness on their QoL for injury, life and roles dimensions were consistent throughout the follow-up period. For example, for the injury domain, outcomes at each follow-up visit (12, 18, 24 and 36 months), as well as the overall follow-up analysis (combining all follow-up visits) were significantly improved from baseline. This in turn suggests that the measured improvement was stable and most likely not the result of placebo, which is known to deteriorate over time.

Although demographic data collected on the overall study cohort were limited, both univariate and multivariate regression were attempted on baseline utility scores using three potential predictors: age, gender and years since the diagnosis of RP, as measured at time of implant (‘years with RP’). Because patients were screened for untreated depression at enrolment, due to the concern that depressed patients may show less motivation to learn how to use the device, this important covariate was not applicable in this population. Furthermore, the population had distributed within each dimension, mean values are provided.

Within each VisQoL dimension, between nine and 20 patients (30 to 67 per cent) reported at least moderate impact of their visual loss on their QoL. The remaining patients self-reported minimal difficulty in performing any given dimension at baseline. Overall, 80 per cent of the cohort reported a significant impact of their vision on QoL at baseline in at least one of the five affected dimensions, confirming that the majority of patients had baseline QoL deficits.

Table 3. Survey scores for patients whose blindness was affecting their quality of life at baseline for relevant dimensions. Scores reflect the average survey score at baseline and the combined average score from 12 to 36 months follow-up visits. Therefore, a decrease in survey score reflects an increase in quality of life. Statistical significance is defined as $p < 0.05$ and is designated with an asterisk.

| VisQoL dimension | Number | % of overall cohort | Baseline mean survey score | Follow-up mean survey score | p-value |
|------------------|--------|---------------------|---------------------------|-----------------------------|---------|
| Injury (item 1)  | 15     | 50                  | 3.8                       | 2.8                         | 0.0362* |
| Life (item 2)    | 20     | 67                  | 4.4                       | 3.7                         | 0.0069* |
| Assistance (item 4) | 9     | 30                  | 3.1                       | 2.4                         | 0.1745  |
| Roles (item 5)   | 16     | 53                  | 4.6                       | 3.8                         | 0.0012* |
| Activity (item 6)| 10     | 33                  | 4.1                       | 3.8                         | 0.1026  |

Figure 1. Normal distribution of Vision and Quality of Life Index (VisQoL) utility scores at baseline. The box-whisker plot at the bottom summarises the VisQoL distribution, where the ‘whisker’ endpoints are the minimum and maximum, the lower and upper ends of the ‘box’ are the first and third quartiles, the mean is located in the middle of the diamond with the ends of the diamond indicating the mean ± 1 standard deviation and the vertical line inside the box indicates the median.

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virtually no identifiable co-morbidities, which are typical in other vision-impaired populations and which can affect QoL (for example, patients with diabetic retinopathy have a high frequency of coronary heart disease, nephropathy or cerebrovascular disease). As already noted, visual acuity (for example, weighted logMAR) was also not a covariate since all patients had uniformly poor baseline vision in both eyes.

Results from the univariate associations with baseline utility scores showed that none of the three potential predictors were statistically significant (Table 4). Multivariate regression tree analysis was completed, forming four groups using gender, age and years with RP (Table 5). The overall $R^2$ (coefficient of determination) was 0.167. Only males under the age of 66 with less than 40 years with RP showed a propensity toward lower baseline utility scores, although the model was inconclusive.

### DISCUSSION

Eighty per cent of patients with RP reported moderate to severe difficulty in one or more VisQoL dimensions pre-implant. In three of the six VisQoL dimensions (injury, life and roles), patients whose blindness was affecting their QoL at baseline showed significant and lasting improvement after implantation with Argus II. In two of the three remaining dimensions (assistance and activity), data appeared to show an improvement, although there was insufficient power to demonstrate significance. In the final VisQoL dimension (friendship), none of the patients reported significant baseline deficits. Overall, the composite utility score showed no significant change.

VisQoL was selected as an instrument for use in the Argus II clinical study because it is vision-specific, easy to administer and gathers utility values. As with other vision-specific instruments, it was both constructed and confirmed in study samples with relatively few patients with significant visual impairment (for example, only nine per cent of vision-impaired patients in the construction study had visual acuity worse than 6/60). Furthermore, there was no indication that the instrument was sensitive to patients with profound low vision or worse. Very recently, a new vision-related QoL questionnaire was developed that is intended for patients with severe loss of vision, which was not available when the study was initiated but which may be a more appropriate instrument for this population.

Relatively little data have been published on the use of VisQoL in a clinical setting. The one notable exception is Fenwick and colleagues, who assessed the impact of diabetic retinopathy and/or macular oedema on VisQoL utility values. In a study cohort of 203 diabetic patients, visual impairment ranged from none (less than 0.18 logMAR) to ‘profound’ (which in their definition was worse than 0.78 logMAR). The authors concluded that the reduction in VisQoL utility scores correlated with profound visual impairment (worse than 0.78 logMAR) but not with mild, moderate or severe visual impairment or disease severity.

In light of the limited sensitivity of VisQoL, it is not surprising that the composite utility score in the Argus II cohort showed no significant improvement over time, even though 33 per cent of patients had significant improvements in visual acuity after three years; however, it was surprising that the baseline utility scores ranged from 0.22 to 0.99, even though all patients had profound low vision (worse than 2.9 logMAR) and were otherwise largely homogeneous (for example, no untreated clinical depression, minimal co-morbidities). Unfortunately, both univariate and multivariate regression were unable to explain the differences, reflecting limited covariates. The high variability among baseline utility scores suggests that patients with RP have varying success in adjusting to profound blindness in different QoL dimensions.

The disparity in baseline utility scores prompted analysis of each VisQoL dimension, considering those patients who self-reported difficulty presented by their loss of vision separately from those who reported no impact of their blindness on QoL. Analysing each individual dimension of a multi-attribute utility score has been recognised as a potentially useful method to identify important changes in patient experiences, particularly as patients value each dimension differently. Furthermore, subdividing each cohort based on pre-treatment QoL values has been adopted in other medical disciplines to establish treatment efficacy.

The level of adjustment or adaptation among patients before treatment is frequently taken into account in studies of populations suffering from chronic disabling diseases, such as cancer, irreversible visual loss and rheumatoid arthritis. The concept is that patients who adapt and therefore accept their disease, will recover some level of normality even before treatment, which equates to higher baseline QoL scores. In contrast, patients who do not adjust to their disease typically have low QoL and frequently a higher incidence of depression.

As adaptation improves over time, particularly with active rehabilitation, QoL may actually be better in end-stage patients, as opposed to patients with a new diagnosis. This in turn may explain why a certain
subset of the Argus II cohort had relatively high QoL values at baseline, even though most patients had a long disease history and the study design excluded patients with significant untreated depression. Thus, considering only the sub-cohort of patients who report moderate to high impact of visual loss at baseline on their QoL is a useful method for determining if a new therapy is efficacious, since only patients with initial low QoL scores can show significant improvement.

Results from analysis of the Argus II cohort identified a significant and lasting improvement for patients whose blindness affected their QoL in three domains: injury, life and roles. In the other two domains for which patients reported difficulty at baseline (assistance and activity), the possible trend was in favour of improvement after implant, although limited power prevented the change from being statistically significant. Patients who reported little or no difficulty at baseline did not show any change or degradation of QoL in any domain.

The stability of QoL improvements within specific domains in Argus II patients is clinically relevant. This point was highlighted in a recent publication by Siqueira and colleagues, wherein NEI-VFQ-25 was used to measure QoL changes in a RP population treated with intravitreal bone-marrow stem cells. Measurements were made at baseline and at three and 12 months after treatment. In a cohort of 20 patients, there was a statistically significant improvement in QoL at three months; however, there was no change relative to baseline at 12 months, suggesting that the benefit was lost over time. It was concluded that the transitory clinical benefit of stem-cell therapy (for example, as observed in other studies investigating its potential) did not persist for three months, which corresponds to the loss in QoL. Therefore, it is reasonable to expect that if clinical benefit were lost over time in those Argus II patients reporting difficulty at baseline, dimension-specific QoL would also deteriorate; however, patients that benefited from use of the Argus II device on this measure maintained that benefit throughout the full follow-up period of 36 months.

The specific relevance of each of the six dimensions measured by VisQoL is difficult to estimate; however, improvement in the injury dimension may have direct impact on the overall health and safety of blind patients. As noted by the developers of the VisQoL instrument, visual impairment is associated with increased risk of falls and hip fractures, among other events. To the degree that Argus II patients feel at less risk of injury as a result of visual impairment, patients will be more self-reliant. This in turn may have considerable utility for both patients and providers.

Data from the injury dimension are also consistent with data on functional vision. Specifically, it was found previously that patients could complete mobility tasks in uncontrolled environments significantly better with the device on versus off. Although baseline functional vision was not measured pre-implant, data confirmed that use of the implant allowed patients to manœuvre across streets and on sidewalks while avoiding obstacles, which is relevant to avoiding injury.

The corresponding improvement in the life and roles VisQoL dimensions also suggests that in patients having difficulty coping with, for example, family and other life demands, treatment with Argus II improves emotional well-being. As with improvements within the injury dimension, it is very significant that the improvement is measured throughout the 36-month follow up.

The lack of patients who report significant impact of their loss of vision within the friendship dimension suggests that patients with advanced RP may have minimal difficulty in developing and/or maintaining interpersonal relationships. This in turn suggests that at least within this population, the friendship dimension is not relevant to establishing utility for any therapy, including the Argus II, as patients have found other means to compensate for vision loss.

Strengths of this study include reporting QoL in patients with profound low vision or worse and measuring QoL after implantation of a novel retinal prosthesis for a full 36 months. Limitations include the small patient population, reflecting the rarity of RP and limited patient information available at baseline for use as possible covariates (including the level of previous rehabilitation, training and support). In particular, understanding the extent of prior rehabilitation would have been helpful in explaining the disparity in baseline utility and domain scores, although this would not have affected the change in QoL scores after treatment.

It is unlikely that any single outcome measure represents a full picture of the benefit of the Argus II system for any particular patient. It is important to note that the VisQoL was one of a battery of visual function and functional vision outcome measures used in this clinical trial, all of which together showed an overall trend of benefit from the Argus II system.

**CONCLUSION**

The VisQoL was used to measure changes in utility scores in a rare population implanted with the Argus II retinal prosthesis system. Utility scores for the overall patient cohort were not significantly different between baseline and follow-up periods; however, patients whose vision negatively affected them with respect to three VisQoL dimensions (injury, life and roles), reported significant and lasting improvement in QoL after implantation of the Argus II retinal prosthesis. No dimensions showed a significant decline in QoL in any sub-cohort. This outcome suggests that individual QoL dimensions may be useful in assessing QoL effects of treatment. These data are consistent with other published outcomes demonstrating that Argus II contributes to improvements in visual acuity and functional vision and further demonstrates that the Argus II treatment can produce significant and lasting improvement in QoL related to the user’s perception of reduced risk of injury, reduced difficulty of meeting the demands of life and reduced difficulty of fulfilling their roles in life.

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**REFERENCES**

1. Chardey GJ, Weiland J, Humayun MS. Artificial vision: needs, functioning and testing of a retinal electronic prosthesis. *Prog Retin Eye Res* 2009; 28: 517–532.
2. Lesis PM, Ackland HM, Lowery AJ et al. Restoration of vision in blind individuals using bionic devices: a review with a focus on cortical visual prostheses. *Brain Res* 2015; 1595: 51–23.
3. Shintani K, Shechtman D, Gurwood A et al. Review and update: current treatment trends for patients with retinitis pigmentosa. *Optometry* 2009; 80: 384–401.
4. Berson EL, Rosen B, Sandberg MA et al. s-3 intake and visual acuity in patients with retinitis pigmentosa receiving vitamin A. *Arch Ophthalmol* 2012; 130: 707–711.
5. Humayun MS, Dorn JD, da Cruz L et al. Interim results from the international trial of Second Sight’s visual prosthesis. Ophthalmology 2012; 119: 779–788.
6. Ho AC, Humayun MS, Dorn JD et al. Long-term results from an epiretinal prosthesis to restore sight to the blind. Ophthalmology 2015; 122: 1547–1554.
7. Geruschat DR, Richards TP, Arditi A et al. An analysis of observer-rated functional vision in patients implanted with the Argus II retinal prosthesis system at three years. Clin Exp Optom 2016; 99: 227–232.
8. Misajon R, Hanthorne G, Richardson J et al. Vision and quality of life: the development of a utility measure. Invest Ophthalmol Vis Sci 2005; 46: 4007–4014.
9. FDA Guidance for Industry. Patient-Reported Outcome Measures: Use in Medical Product Development to Support Labelling Claims. 2009 [cited 2016 February 25]. Available at: http://www.fda.gov/downloads/Drugs/Guidances/UCM193282.pdf.
10. Sugawara T, Hagiwara A, Hiramatsu A et al. Relationship between peripheral visual field loss and vision-related quality of life in patients with retinitis pigmentosa. Eye 2010; 24: 535–539.
11. Burstedt M, Monestam E. Self-reported quality of life in patients with retinitis pigmentosa and maculopathy of Bothnia type. Clin Ophthalmol 2010; 4: 147–154.
12. Peacock S, Misajon R, Izrai A et al. Vision and quality of life: development of methods for the VisQoL vision-related utility instrument. Ophthalmic Epidemiol 2008; 15: 218–223.
13. The VisQoL scoring algorithm [cited 2015 October 28]. Available at: http://www.aqol.com.au/index.php/scoringalgorithm.id=188.
14. Hahn B, Shin Y, Shim E et al. Depression and the vision-related quality of life in patients with retinitis pigmentosa. Br J Ophthalmol 2008; 92: 600–605.
15. Alcubierre N, Rubinat E, Travasat A et al. A prospective cross-sectional study on quality of life and treatment satisfaction in type 2 diabetic patients with retinopathy without other major late diabetic complications. Health Qual Life Outcomes 2014; 12: 131.
16. Misajon R, Hanthorne G, Richardson J et al. Vision and quality of life: the development of a utility measure. Invest Ophthalmol Vis Sci 2005; 46: 4007–4014.
17. Finger RP, Tellis B, Crewe J et al. Developing the impact of vision impairment—very low vision (IVI-VLV) questionnaire as part of the LoVADA protocol. Invest Ophthalmol Vis Sci 2014; 55: 6150–6158.
18. Fensstic F, Zia J, Pesudos K et al. Assessing disutility associated with diabetic retinopathy, diabetic macular oedema and associated visual impairment using the vision and quality of life index. Clin Exp Optom 2012; 95: 362–370.
19. Feeny D. A utility approach to the assessment of health-related quality of life. Med Care 2000; 38: 151–154.
20. Nieuwkerk P, Gisolf E, Colebunders R et al. Quality of life in adaptive- and non-adaptive HIV infected patients in trial of ritonavir/saquinavir therapy. AIDS 2000; 14: 181–187.
21. Decat Bergerot C, Cavalcanti Ferreira de Araujo TC. Assessment of distress and quality of life of cancer patients over the course of chemotherapy. Invest Educ Enferm 2014; 32: 216–224.
22. Siqueira R, Messias A, Messias K et al. Quality of life in patients with retinitis pigmentosa submitted to intravitreal use of bone marrow-derived stem cells (Reticell-clinical trial). Stem Cell Res Ther 2015; 6: 29.
23. Kostova Z, Caiata-Zufferery M, Schulz PJ. The process of acceptance among rheumatoid arthritis patients in Switzerland: A qualitative study. Pain Res Manage 2014; 19: 61–68.