## Title

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# Development of a Patient-Reported Outcome Measure to Assess Symptoms Associated with Cataract Surgery and Intraocular Lens Implants

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***Purpose:*** To develop a standardized patient-reported outcome measure of visual perceptions and symptoms for implanted premium and monofocal intraocular lenses (IOLs).

***Design:*** Observational study before and after IOL implants to assess the measure and symptom experience.

***Participants:*** Adults scheduled for binocular implantation of the same IOL type completed the survey at baseline prior to surgery (n = 716) and postoperatively (n = 554). Most respondents were female (64%), White (81%), 61 or older (89%), and had some college or more education (62%).

***Methods:*** Administration was by web survey with mail follow-up and phone reminders.

***Main Outcome Measures:*** Frequency, severity, and level of symptom bother in the last 7 days for 14 symptoms: (1) glare, (2) hazy vision, (3) blurry vision, (4) starbursts, (5) halos, (6) snowballs, (7) floaters, (8) double images, (9) rings and spider webs, (10) distortion, (11) light flashes with eyes closed, (12) light flashes with eyes open, (13) shimmering images, and (14) dark shadows.

***Results:*** The median correlation among having 14 symptoms at baseline was only 0.19. Mean uncorrected binocular visual acuity improved from a preoperative value of 0.47 logarithm of the minimum angle of resolution (logMAR; Snellen 20/59) to a postoperative value of 0.12 (20/26) and best-corrected binocular visual acuity improved from 0.23 logMAR (20/34) preoperative to 0.05 logMAR (20/22) postoperative. The most bothersome symptoms were reduced after surgery: preoperative/postoperative glare (84%/36%), blurry vision (68%/22%), starbursts (66%/28%), hazy vision (63%/18%), snowballs (55%/17%), and halos (52%/22%). All symptoms decreased significantly ($P < 0.0001$) from before to after surgery except for dark crescent-shaped shadows (4%/4%). The percentage of symptoms rated as quite a bit or extremely bothersome declined from before to after surgery except for dark crescent-shaped shadows (29%/32%): blurry vision (54%/15%), snowballs (52%/14%), glare (49%/15%), and halos (46%/14%). Having monofocal IOL implants was associated with significantly more reduction in halos, starbursts, glare, and rings and spider webs, but less improvement in self-reported general vision.

***Conclusions:*** This study provides support for the 37-item Assessment of IntraOcular Lens Implant Symptoms (AIOLIS) instrument for use to assess symptoms and general perceptions of vision in clinical studies and clinical care.

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Intraocular lens (IOL) implants are artificial lenses that can be used to replace the natural lens of the eye and are considered by the United States Food and Drug Administration (FDA) as high risk. FDA's device classification is risk based, that is, the risk the device poses to the patient and/or the user is a major factor in the class it is assigned.[1] Class I includes devices with the lowest risk and class III includes those with the greatest risk. IOLs fall under the category of class III devices. Approximately 14% of cataract patients receive premium IOLs.[2] Premium IOLs "correct more than the spherical error at distance, include multifocal, accommodating, toric, and phakic IOLs."[2] Adverse events associated with multifocal IOLs such as glare, halos, and loss of contrast sensitivity have been documented.[3–5] The FDA/American Academy of Ophthalmology Developing Novel Endpoints for Premium IOLs


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Workshop report noted that there is insufficient information about adverse events associated with premium IOLs and suggested that there was a need for patient-reported outcome measures.[2]

This paper describes the development of a patient-reported outcome measure to assess symptoms relevant to patients receiving IOL implants. We followed the recommendations in the FDA guidance document for developing patient-reported outcome instruments.[6] The Assessment of IntraOcular Lens Implant Symptoms (AIOLIS) survey is intended for use in clinical studies and clinical care to assess change in ocular symptoms associated with IOLs, including IOLs that patients use for near, intermediate, and distance vision.

## Methods

This study was approved by the UCLA Human Subjects Committee (IRB#17-000146) and the RAND Human Subjects Committee (IRB#2018-1047-AM01) and was performed in accordance with the tenets of the Declaration of Helsinki. We reviewed the literature on the development and use of patient-reported measures for patients with IOLs, searching PubMed using a variety of keywords including *patient-reported*, *visual symptoms*, *health-related quality of life*, and *patient satisfaction* in combination with *cataracts*, *eye disease*, *visual aberrations*, *dysphotopsias*, *flashes*, *light arcs*, *halos*, *light streaks*, *flickering*, *shimmering*, *dark shadows*, and *vision*. Then, we conducted 13 focus groups with a total of 93 adults (87 in English and 6 in Spanish) who had undergone cataract surgery and obtained IOLs within the last 12 months. Focus groups were held in 5 locations: Los Angeles, California; Pasadena, California; San Antonio, Texas; Miami, Florida; and Baltimore, Maryland. The focus groups were led by experienced survey researchers using a semi-structured guide. The focus groups were audiotaped and transcribed. We asked focus group participants about the impact of their vision on multiple areas of their life. Some examples of the probes used include the following:

1. Are there things that you are unable to do because of your vision?
2. How does life now compare to the way it was before you got your intraocular lenses following cataract surgery?
3. What are the most important effects of your intraocular lenses on your life?
4. What things do you do to try to cope with problems you have with your vision?
5. What were your expectations about your intraocular lenses before you had cataract surgery? Were these expectations met?
6. Have you had any unexpected problems with your intraocular lenses?
7. What are your expectations regarding your intraocular lenses going forward?

After the open-ended questions, we asked participants what they thought of various images depicting visual symptoms and existing questionnaire items assessing symptoms and spectacle independence (e.g., How well do these questions represent the impact of vision on your life?). Two of the most common issues mentioned by focus group participants were difficulty reading small print (e.g., on a medicine bottle) and difficulty driving at night. Frequent comments mentioned about the impact of having surgery and placement of the IOL implants were that they no longer needed to wear glasses, were more independent, and able to drive again at night.

Based on the literature review and focus groups, we drafted items assessing visual symptoms (flashes, light arcs, halos, light streaks, flickering/shimmering, and dark shadows) and difficulty with daily tasks such as driving during the day, driving at night, reading a newspaper or book, reading on a smartphone, and reading on a computer. We conducted a total of 19 cognitive interviews (14 in English and 5 in Spanish) using intermittent probes with draft items. In the interviews, we probed about item stem content and clarity of the response options. We revised survey items based on the cognitive interviews in preparation for the field test.

### Field Test Eligibility

The field test targeted adults 45 years of age and older who were scheduled for binocular implantation of the same IOL type. Eligible IOLs included: (1) accommodative, (2) extended depth of focus, (3) monofocal, (4) multifocal, (5) toric accommodative, (6) toric extended depth of focus, (7) toric monofocal, (8) toric multifocal, and (9) trifocal. The dominant eye was targeted for emmetropia, and the non-dominant eye could be targeted for emmetropia or up to −0.75 diopter (D) of myopia. In addition, the potential visual acuity was preoperatively estimated to be 20/30 or better after cataract removal and IOL implantation, based on potential acuity meter or pinhole test for near vision.

### Field Test Survey

The preoperative survey included 86 questions that assessed the frequency, severity, and level of bother in the last 7 days of 14 symptoms: (1) glare, (2) hazy vision, (3) blurry vision, (4) starbursts, (5) halos and spider webs, (6) snowballs, (7) floaters, (8) double images, (9) rings and spider webs, (10) distortion, (11) light flashes with eyes closed, (12) light flashes with eyes open, (13) shimmering images, and (14) dark shadows (see images, Appendix A, available at www.aaojournal.org). The questions were preceded by a definition of the symptom and a color photograph depicting the symptom (except for shimmering images). The survey assessed when symptoms occurred: when wearing versus not wearing glasses or contact lenses and at different times of the day.

The survey asked patients to rate their vision as poor, fair, good, very good, or excellent. They were asked: How satisfied are you with your vision right now? 1 (completely dissatisfied) to 6 (completely satisfied). We created a 5-item general ratings of vision scale (internal consistency reliability[6] = 0.79) consisting of these 2 questions and 3 others: (1) self-rating of uncorrected vision; (2) self-rating of distance vision; and (3) self-rating of intermediate vision. The simple-summated version of this 5-item scale had a product-moment correlation of 0.95 before surgery and 0.97 postoperatively with scores estimated using item response theory (Rasch and graded response models).

The postoperative survey included the same questions as the preoperative survey and 2 retrospective change items: (1) Compared to before you had cataract surgery, how are your visual symptoms now? and (2) Compared to before you had cataract surgery, how is your vision now? Both questions were administered using a 5-category response scale: much better, a little better, about the same, a little worse, and much worse. This survey also asked whether cataract surgery was delayed because of the COVID-19 pandemic, and whether it affected the care received from the doctor who performed the surgery. In addition, the survey asked if a lens was implanted in both eyes, your right eye, or your left eye.

### Field Test Survey Administration

The preoperative survey was self-administered about 45 days prior to surgery in English or Spanish. Surveys were distributed by personnel at 20 sites and patients were asked to complete them and mail these to the investigators. A post-paid incentive of $20 United States dollars was offered. A majority of those who completed the survey completed it at home (75%) while the others (25%) completed it in the eye doctor's office.

The postoperative survey was administered after surgery for the second eye, about 4−6 months after the preoperative survey. This survey was administered on the web with mail follow-up and phone reminders to non-respondents. A post-paid incentive of $35 United States dollars was offered for completing the postoperative survey. Most of the respondents completed the survey by web (62%) and the other 38% completed a paper survey. At the time of completing the postoperative survey, 94% of the respondents reported that they had cataract surgery and a lens implanted in both eyes. The median self-reported time to complete the follow-up survey was 9.5 minutes with a mode of 10 minutes (mode reported by 37%).

### Clinical Measures

Postoperative uncorrected and corrected binocular visual acuity, manifest refractive error, and surgical and postoperative complications were recorded by representatives at each site.

### Method of Data Analysis

We report the number of surveys completed prior to surgery (baseline), postoperative survey participation rate, item missing data rates for the surveys, and characteristics of the sample. Next, we provide estimates of the prevalence of the 14 ocular symptoms at baseline and postoperatively, and correlations between having each symptom at baseline and postoperatively. We also report Spearman correlations among the frequency of each the 14 symptoms and estimate internal consistency reliability[7] for a 14-item symptom scale. Then, we report frequencies for reported severity and the extent to which each symptom bothered the patient (level of symptom bother), time of the day when symptoms were experienced, and when wearing and when not wearing corrective lenses. Next, we estimate product-moment correlations of symptom severity and level of symptom bother with self-ratings of vision, satisfaction with vision, and ability to see without correction. Then, we report associations of having individual symptoms with dissatisfaction with vision postoperatively and examine associations between change in symptoms with change in the 5-item general rating of vision scale. Next, we estimate product-moment correlations of change in symptoms and change in the general ratings of vision scale with type of IOL (monofocal versus multifocal) and by postoperative manifest refraction (hyperopia, myopia, and astigmatism). Finally, we evaluate responsiveness to change in reports of symptom frequency based on a retrospective rating of change in symptoms item.

Statistical analyses were conducted using SAS version 9.4 (TS1M6) software (2010; SAS Institute).[8]

## Results

### Survey Completion and Missing Data

The baseline survey was administered to 716 patients before surgery and 554 (77%) of those completed the postoperative survey. Of the 27 questions asked of all respondents (i.e., no skip patterns) at baseline, 75% had no missing data, 11% had one missing item, 6% had 2 missing items, 2% had 3 missing items, and 6% were missing 4 or more items. For the follow-up survey, 82% had no missing data, 6% had 1 missing item, 6% had 2 missing items, 1% had 3 missing items, and 5% were missing 4 or more items.

### Sample Characteristics

Characteristics of the field test study participants who completed the baseline survey before surgery and those completing a postoperative survey were similar and are provided in Table 1. The majority of those providing baseline survey data were female (64%), non-Hispanic White (81%), 61 years of age or older (89%), and had some college or greater education (62%). Mean preoperative best uncorrected binocular distance visual acuity was 0.47 logarithm of the minimum angle of resolution; (logMAR; 20/59 Snellen visual acuity) and best-corrected binocular visual acuity was 0.23 logMAR (20/34 Snellen visual acuity). As expected, visual acuity improved postoperatively. Satisfaction with vision increased from baseline to postoperatively by an average of 2 response categories. Satisfaction at baseline was not significantly correlated with satisfaction postoperatively ($r = -0.05$; $P = 0.2374$). Satisfaction with vision improved at all 20 clinical sites but varied significantly by site: $F(19,527) = 2.52$ ($P < 0.0004$), and ranged from 0.8 to 3.2 points. Owing to the COVID-19 pandemic, 6% of the sample reported having an IOL implant in only a single eye at the time of survey completion.

Frequency of wearing glasses or contact lenses in the last 7 days before (after) surgery was: 63% (15%) all of the time, 16% (17%) most of the time, 10% (32%) some of the time, 4% (15%) a little of the time, and 6% (21%) did not wear glasses or contact lenses. Most study participants wore glasses or contact lenses before surgery for reading, watching television, and driving, but after surgery, correction was used only for reading by most of the participants.

Sixteen percent of the respondents to the follow-up survey reported that their cataract surgery was delayed due to the COVID-19 pandemic. Five percent stated that the pandemic made their care a little worse and one percent indicated a lot worse.

### Symptom Frequencies

Table 2 and Figure 1 provide the percentage of the longitudinal participants (i.e., those who completed both a baseline and postoperative survey) reporting each of the 14 ocular symptoms. The symptoms are listed in order of decreasing prevalence at baseline, prior to surgery. The prevalence of the most common preoperative symptoms reduced postoperatively: glare (preoperative/postoperative 84%/36%), blurry vision (68%/22%), starbursts (66%/28%), hazy vision (63%/18%), snowballs (55%/17%), and halos (52%/22%). The least prevalent symptoms were shimmering images (8%) and dark crescent-shaped shadows (4%). The median correlation among having each of the 14 symptoms (0 = do not have the symptom, 1 = have the symptom) was only 0.19 at baseline and 0.17 postoperative, indicating that the items yield substantially unique information. Internal consistency reliability of the 14 symptoms was 0.74 and item-total correlations ranged from 0.24 (blurry vision) to 0.47 (halos). The small correlations found among symptoms support examining them separately.

The percentage of all symptoms decreased significantly ($P < 0.0001$) from before to after surgery, except for dark crescent-shaped shadows, which were uncommon preoperatively and postoperatively (4% at both time points). The phi coefficients in Table 2 indicate the correlations (equivalent to product-moment correlations) between having symptoms before versus after surgery. All correlations except for rings and spider web symptoms

Table 1. Characteristics of Field Test Participants

| Characteristic | Baseline (n = 716) | After Surgery (n = 554) |
|---|---|---|
| Female sex | 64% | 65% |
| Race and ethnicity | | |
| Hispanic | 9% | 7% |
| White | 81% | 84% |
| Black | 6% | 5% |
| Asian | 2% | 2% |
| Other | 2% | 2% |
| Age (yrs) | | |
| 31–40 | 0.3% | 0.2% |
| 41–50 | 2% | 1% |
| 51–60 | 9% | 7% |
| 61–70 | 38% | 37% |
| ≥ 71 | 51% | 54% |
| Education | | |
| Eighth grade or less | 2% | 2% |
| Some high school | 7% | 5% |
| High school graduate | 30% | 29% |
| Some college | 32% | 32% |
| 4-yr college degree | 12% | 12% |
| > 4-yr degree | 18% | 19% |
| Spanish language survey | 5% (n = 34) | 3% (n = 17) |
| Paper questionnaire | 100% | 38% |
| Web administered | 0% | 62% |
| Best uncorrected binocular visual acuity (logMAR) | n = 346 | n = 404 |
| Mean | 0.47 | 0.12 |
| SD | 0.35 | 0.16 |
| Range | 0–> 1.90 | −0.10 to > 1.24 |
| Best corrected binocular visual acuity (logMAR) | n = 597 | n = 391 |
| Mean | 0.23 | 0.05 |
| SD | 0.18 | 0.12 |
| Range | −0.12 to > 1.48 | −0.20 to > 1.24 |
| Spherical equivalent manifest refractive error (diopters) | | |
| Left eye | | |
| Mean | −0.77 | −0.02 |
| SD | 3.23 | 0.82 |
| Right eye | | |
| Mean | −1.35 | 0.06 |
| SD | 9.39 | 0.83 |

logMAR = logarithm of the minimum angle of resolution; SD = standard deviation.
Characteristics of those completing the baseline survey and the post-surgery survey are shown. Seventy-six percent of paper questionnaires at baseline were completed in the doctor's office. We imputed best uncorrected visual acuity for 2 patients who had improbable values (i.e., logMAR, 4) using best corrected visual acuity (predicted = 0.00789 + 0.07707 × corrected visual acuity).

were statistically significant but small in magnitude, indicating variance in who had a symptom at baseline and postoperatively. Note that 23 of the 32 (72%) people who reported crescent-shaped shadows before surgery also reported floaters; 17 of the 25 (68%) who reported shadows after surgery also reported floaters.

Table 3 shows that from 2% (shimmering images) to 20% (starbursts) of study participants who reported not having a symptom prior to surgery reported it postoperatively. Conversely, from 12% (shimmering images) to 53% (floaters) of those who reported a symptom prior to the surgery indicated that they no longer had the symptom after surgery.

## Symptom Severity

The self-reported severity of symptoms before and after surgery is provided in Table 4 and in Figure 2. The most common reports of the most severe symptoms preoperatively were reduced postoperatively including halos (preoperative/postoperative, 27%/5%), glare (26%/6%), snowballs (24%/3%), blurry vision (23%/6%), and hazy vision (23%/5%). Among those reporting a symptom postoperatively, the highest percentage perceived to be severe was for dark crescent-shaped shadows (17%). However, only 4% of patients reported having this symptom both preoperatively and postoperatively as noted previously.

## Level of Symptom Bother

As seen in Table 5 and Figure 3, the greatest level of symptom bother (reporting either quite a bit or extremely bothered) comparing preoperative to postoperative was reported for blurry vision (preoperative 54%/postoperatively 15%), snowballs (52%/14%), glare (49%/15%), and halos (46%/14%). The level of bother of all symptoms declined from before to after surgery except for dark crescent-shaped shadows (10%/12%).

## Time of Day When Symptoms Were Experienced

The time of the day when symptoms were experienced was similar before and after surgery (Table 6). The symptoms that occurred more often during the day were blurry vision, hazy vision, floaters, double images, distortion, shimmering images, and dark crescent-shaped shadows. Symptoms experienced more often during the night were glare, starbursts, snowballs, halos, and rings and spider webs.

## Corrective Lenses and Symptoms

Table 7 shows whether symptoms occurred when wearing correction (glasses or contacts) and when not wearing correction. Before surgery, for most people symptoms occurred when wearing and when not wearing corrective lenses. After surgery, there was a much greater percentage of those having a symptom reporting it happening when not wearing glasses or contact lenses.

Correlations of Symptom Severity and Level of Symptom Bother with General Ratings of Vision

Preoperatively 35% of the sample reported that their vision was poor, 49% fair, 15% good, and 1% very good or excellent. After surgery, 2% reported their vision as poor, 7% fair, 26% good, 46% very good, and 19% excellent. Satisfaction with vision before (after) surgery was as follows: 14% (3%) completely dissatisfied, 34% (8%) very dissatisfied, 35% (5%) somewhat dissatisfied, 15% (22%) somewhat satisfied, 2% (41%) very satisfied, and 1% (21%) completely satisfied. Before surgery, 79% of the sample rated how well they were able to see without corrective devices to be not very well, 20% pretty well, and 1% very or perfectly well before surgery. After surgery, 11% reported not very well, 34% pretty well, and 54% very well or perfectly well.

Table 8 reports product-moment correlations before surgery (baseline) between self-reports of symptom severity and level of symptom bother with self-reported vision, satisfaction with vision, and ability to see without correction. Product-moment correlations with self-reported level of symptom bother tended to be a little larger than correlations with self-reported symptom severity. Correlations between self-reported severity and level of symptom bother at baseline ranged from 0.64 (shimmering images) to 0.78 (halos); the median correlation was 0.73.

Table 2. Percentage of Sample Reporting Symptoms Before and After Surgery

| Symptom | Preoperative | Postoperative | *t* Test | Coefficient |
|---|---|---|---|---|
| Glare | 84% | 36% | 14.48 | 0.14 |
| Blurry vision | 68% | 22% | 18.32 | 0.15 |
| Starbursts | 66% | 28% | 14.31 | 0.11 |
| Hazy vision | 63% | 18% | 18.43 | 0.15 |
| Snowballs | 55% | 17% | 15.66 | 0.20 |
| Halos | 52% | 22% | 11.62 | 0.14 |
| Floaters | 49% | 35% | 5.92 | 0.37 |
| Double images | 29% | 9% | 9.89 | 0.26 |
| Rings and spider webs | 29% | 11% | 7.68 | 0.06* |
| Flash with eyes closed | 18% | 8% | 4.88 | 0.17 |
| Distortion | 17% | 6% | 6.50 | 0.17 |
| Flash with eyes open | 17% | 9% | 4.02 | 0.13 |
| Shimmering images | 8% | 3% | 4.08 | 0.17 |
| Dark crescent-shaped shadow | 4% | 4% | 0.00 | 0.09† |

Restricted to longitudinal sample. Percentage with all symptoms except dark crescent-shaped shadow decreased significantly ($P < 0.0001$).
*Not significant.
†$P < 0.05$ (all other coefficients significant at $P < 0.01$).

## Associations of Symptoms with Satisfaction with Vision

Dissatisfaction with vision postoperatively was significantly related in bivariate analyses (product-moment correlations) to having 9 symptoms: (1) blurry vision ($r = 0.19$); (2) distortion ($r = 0.19$); (3) double images ($r = 0.15$); (4) shimmering images ($r = 0.14$); (5) hazy vision ($r = 0.14$); (6) flash with eyes open ($r = 0.14$); (7) rings and spider webs ($r = 0.14$); (8) halos ($r = 0.11$); and (9) crescent-shaped shadows ($r = 0.11$).

In an ordinary least squares regression mode, 22% of the variance in change in satisfaction with vision was explained by change in individual symptoms, demographics (gender, race, age, and education), and whether the patient received help completing

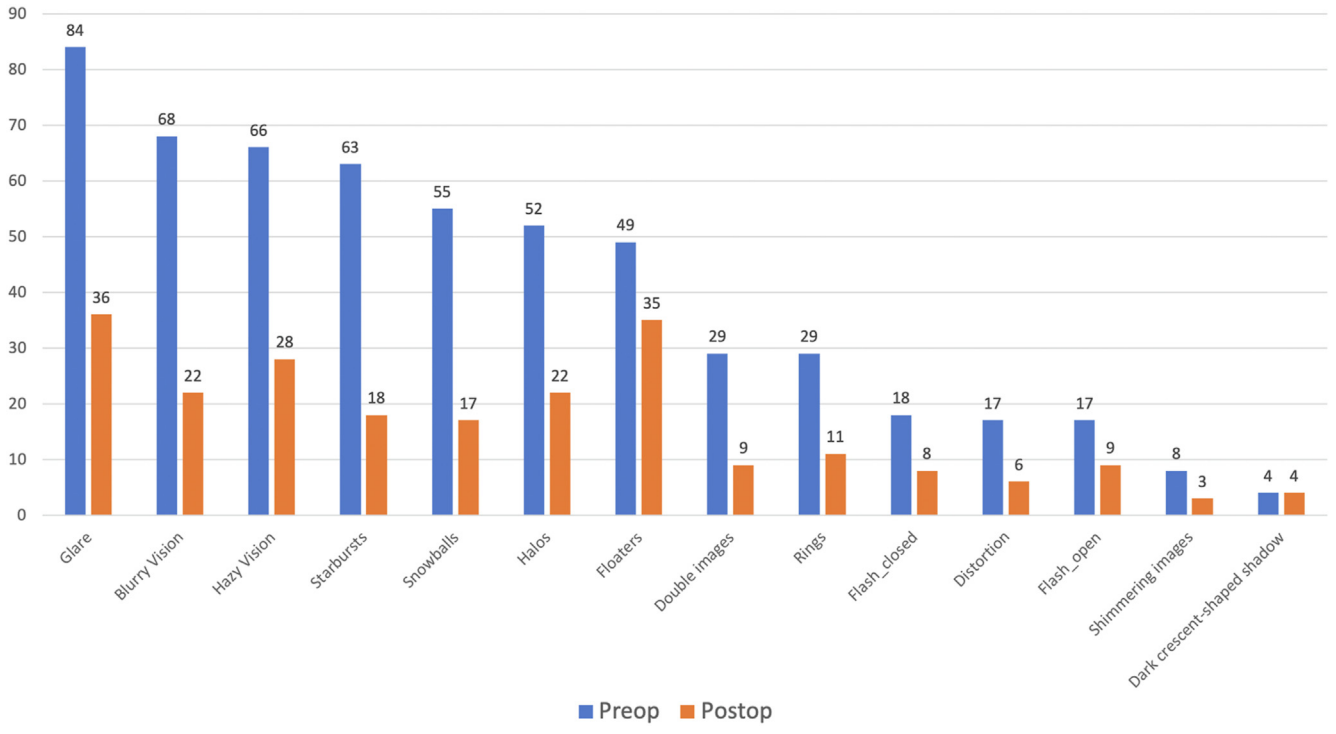


**Figure 1.** Bar graph showing results for the question: In the last 7 days, how often did you see . . . ?

Table 3. Changes between Not Having and Having Symptoms before and after Surgery

| Symptom | Did Not Have before, But Had after Surgery | Had before, But Did Not Have after Surgery |
|---|---|---|
| Glare | 19% | 38% |
| Blurry vision | 13% | 26% |
| Starbursts | 20% | 31% |
| Hazy vision | 9% | 22% |
| Snowballs | 9% | 24% |
| Halos | 16% | 28% |
| Floaters | 18% | 53% |
| Double images | 4% | 20% |
| Rings and spider webs | 10% | 14% |
| Flash with eyes closed | 6% | 18% |
| Distortion | 4% | 14% |
| Flash with eyes open | 7% | 18% |
| Shimmering images | 2% | 12% |
| Dark crescent-shaped shadow | 4% | 14% |

Restricted to longitudinal sample.

the baseline survey. There were 3 significant independent variables (standardized estimates): increase in blurry symptoms ($\beta = -0.20$), increase in snowballs ($\beta = -0.16$), and White race ($\beta = 0.09$).

### Associations of Change in Symptoms with 5-Item General Ratings of Vision Scale

Twenty-four percent of the adjusted variance in change in the 5-item general rating of vision scale was accounted for (standardized β values provided within parentheses) by best-corrected visual acuity postoperatively (−0.16), change in blurry vision (−0.29), snowballs (−0.23), and hazy vision (−0.14), controlling for mode of administration postoperatively. Having received an IOL implant in both eyes was positively associated with the general rating of vision scale at $r = 0.12$ ($P = 0.0074$), reductions in starbursts ($r = -0.15$; $P = 0.0011$), and distortion ($r = -0.10$; $P = 0.0335$), but it was not significantly associated with change in the other 12 symptoms.

### Associations of Type of IOL (Monofocal vs Multifocal) and Manifest Refraction with Symptoms and 5-Item General Ratings of Vision Scale

We examined associations of monofocal versus multifocal IOL implant with change in symptoms and in the general vision scale. Having monofocal IOL implants was associated with significantly more reduction in halos ($t = 3.11$; $P = 0.0020$), starbursts ($t = 2.49$; $P = 0.0134$), glare ($t = 3.78$; $P = 0.0002$), and rings and spider webs ($t = 4.69$; $P < 0.0001$), but less improvement in self-reported general vision ($t = -2.00$; $P = 0.0463$). Type of IOL was not significantly associated with change in the other 10 symptoms or change in best-corrected visual acuity.

Myopia (spherical equivalent $\leq -0.50$ D in either eye), hyperopia (spherical equivalent $\geq +0.50$ D in either eye), and astigmatism (magnitude of cylinder error of $\geq 0.50$ D absolute value at any axis) were examined postoperatively. Hyperopia was significantly associated with worse self-reported general vision ($r = -0.20$; $P = 0.0242$) and less satisfaction with vision ($r = -0.23$; $P = 0.0079$), but was not correlated with dependence on corrective lenses. Myopia was not significantly associated with general vision, satisfaction with vision, or dependence on corrective lenses. Astigmatism was significantly associated with worse self-reported general vision ($r = -0.29$ and $r = -0.21$ in left and right eyes, respectively) and dependence on corrective lenses ($r = -0.39$ and $r = -0.24$ for left and right eyes, respectively). Hyperopia, myopia, and astigmatism were not significantly associated with visual symptoms, adjusting for multiple comparisons using Duncan's multiple range test.

### Responsiveness of Symptoms to Change

Change in the frequency of 14 symptoms was significantly associated with the retrospective rating of change asked postoperatively (Compared to before you had cataract surgery, how are your visual symptoms now?): $F(4,497) = 9.15$ ($P < 0.0001$). The change in symptoms was monotonically related to the retrospective change item with a mean increase of 0.39 standard deviation (SD) in symptoms for those reporting they were much worse and a decrease of 1.06 SD for those reporting they were much better.

## Discussion

The AIOLIS instrument was developed following FDA's guidance document on Patient-Reported Outcomes[6] and was evaluated in a large field test sample. We conducted 13 focus groups and then 19 cognitive interviews clarifying response options prior to the field test. The use of photographic images and standardized instructions on how to present the questionnaire are a strength of the study. Many of these sites had been previously involved in conducting clinical studies used to support FDA submissions and have experience in standardizing vision testing. We provided instructions to sites on the collection of clinical data. The use of several independent sites contributed to variability of the visual acuity and refractive data, but enhanced the generalizability of the findings and insights for future administration of the survey. The COVID-19 pandemic made collecting data more difficult with surgical and follow-up delays. However, the use of both a web and paper survey increased the

Table 4. Self-reported Severity of Symptoms before and after Surgery

| Symptom | Mild | Moderate | Severe |
|---|---|---|---|
| Glare | 18% (57%) | 56% (37%) | 26% (6%) |
| Blurry vision | 26% (72%) | 51% (22%) | 23% (6%) |
| Starbursts | 31% (66%) | 54% (28%) | 15% (6%) |
| Hazy vision | 24% (59%) | 53% (36%) | 23% (5%) |
| Snowballs | 25% (61%) | 51% (35%) | 24% (3%) |
| Halos | 29% (61%) | 44% (33%) | 27% (5%) |
| Floaters | 56% (70%) | 38% (24%) | 6% (5%) |
| Double images | 31% (66%) | 48% (32%) | 21% (2%) |
| Rings and spider webs | 30% (55%) | 51% (38%) | 18% (7%) |
| Flash with eyes closed | 54% (73%) | 40% (23%) | 6% (5%) |
| Distortion | 30% (62%) | 55% (31%) | 15% (6%) |
| Flash with eyes open | 38% (74%) | 50% (24%) | 12% (2%) |
| Shimmering images | 44% (60%) | 49% (33%) | 7% (7%) |
| Dark crescent-shaped shadow | 27% (58%) | 55% (25%) | 18% (17%) |

After surgery data shown within parentheses.

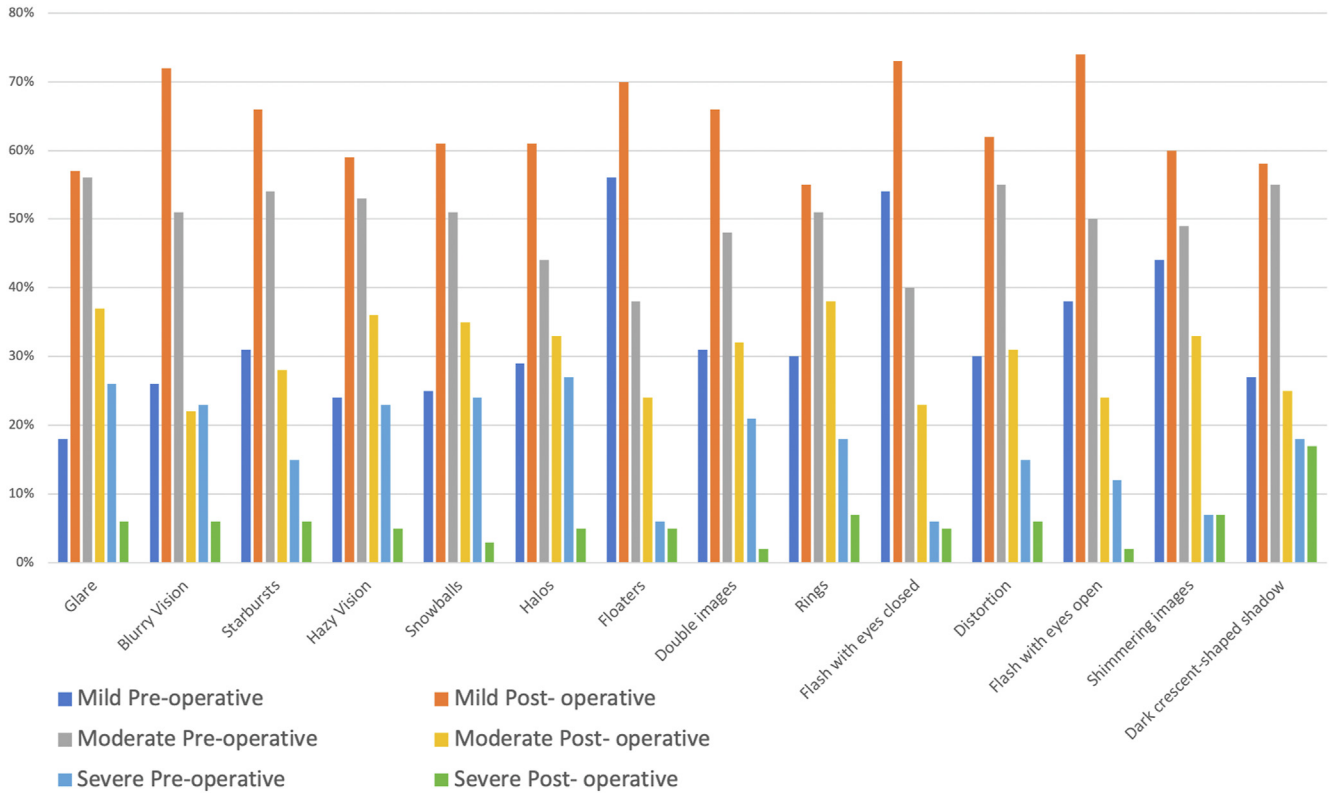


**Figure 2.** Bar graph showing the severity of symptoms before and after surgery.

opportunities for patients to complete the survey post-operatively. Eighty-six percent to 88% of the respondents had only 1 missing answer out of 27 questions asked on both preoperative and postoperative surveys.

Before surgery, more than half the sample reported glare (84%), blurry vision (68%), starbursts (66%), hazy vision (63%), snowballs (55%), and halos (52%) and the least prevalent symptoms were shimmering images (8%) and dark crescent-shaped shadows (4%; Table 2). The percentage of all symptoms except dark crescent-shaped shadows decreased significantly ($P < 0.0001$) from before to after surgery. The greatest level of symptom bother (reporting either quite a bit or extremely bothered) at baseline was reported for blurry vision (54%), snowballs (52%), glare (49%), and halos (46%). The level of bother of all symptoms declined from before to after surgery except for dark crescent-shaped shadows. Although this symptom was infrequent at 4% postoperatively, it is worth noting that

Table 5. Symptom Bother before and after Surgery

| Symptom | Not at All | A Little | Somewhat | Quite a Bit | Extremely |
|---|---|---|---|---|---|
| Glare | 2% (15%) | 19% (46%) | 30% (24%) | 36% (12%) | 13% (3%) |
| Blurry vision | 1% (4%) | 18% (50%) | 28% (31%) | 37% (11%) | 17% (4%) |
| Starbursts | 1% (12%) | 25% (45%) | 32% (25%) | 29% (12%) | 13% (5%) |
| Hazy vision | 3% (22%) | 18% (44%) | 36% (23%) | 33% (9%) | 10% (2%) |
| Snowballs | 3% (18%) | 19% (39%) | 26% (30%) | 38% (11%) | 14% (3%) |
| Halos | 4% (21%) | 19% (42%) | 32% (24%) | 32% (11%) | 14% (3%) |
| Floaters | 15% (29%) | 43% (41%) | 25% (19%) | 13% (8%) | 4% (2%) |
| Double images | 2% (11%) | 19% (48%) | 33% (34%) | 32% (5%) | 4% (3%) |
| Rings and spider webs | 3% (15%) | 25% (52%) | 34% (18%) | 28% (12%) | 15% (3%) |
| Flash with eyes closed | 12% (24%) | 42% (51%) | 25% (20%) | 15% (4%) | 10% (0%) |
| Distortion | 1% (9%) | 21% (44%) | 40% (25%) | 25% (19%) | 5% (3%) |
| Flash with eyes open | 2% (22%) | 28% (51%) | 35% (18%) | 24% (8%) | 13% (2%) |
| Shimmering images | 5% (12%) | 28% (38%) | 53% (38%) | 9% (6%) | 11% (6%) |
| Dark crescent-shaped shadow | 5% (12%) | 19% (40%) | 48% (16%) | 19% (20%) | 10% (12%) |

After surgery data shown within parentheses.

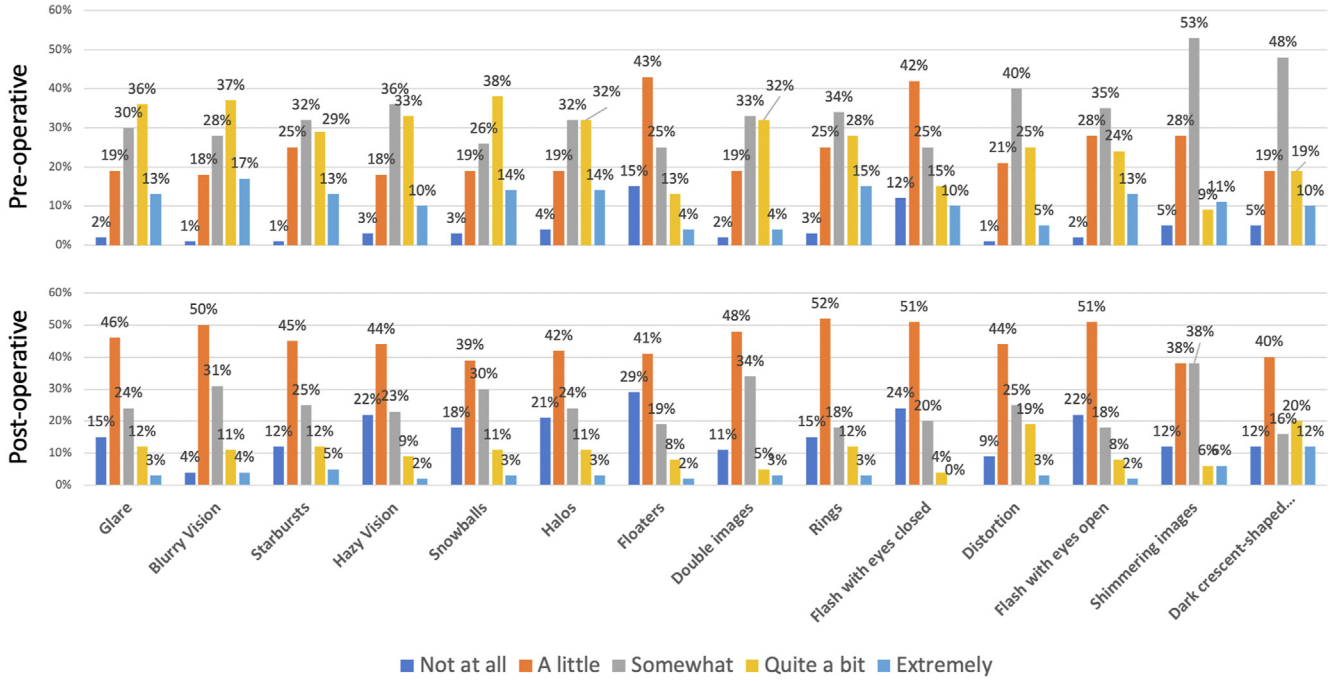


**Figure 3.** Bar graphs showing symptom bother before and after surgery.

it was associated with a high level of symptom bother (17%) following surgery; it is likely that this symptom reflects the clinical manifestation of negative dysphotopsia. Wearing monofocal IOL implants and hyperopia were associated significantly with worse self-reported general vision. Also, consistent with Schallhorn et al,[9] our study found that astigmatism was negatively associated with self-reported general vision.

The level of symptom bother was highly correlated with perceived severity. Given the large empirical overlap, the final AIOLIS includes level of symptom bother, but not symptom severity. Glare and associated symptoms including snowballs, halos, starbursts, and rings and spider webs were far less common (< 20%) during the day but much more commonly observed at night (> 50%) both before and after surgery (Table 6). Hence, including both questions about frequency and level of bother of glare during the day and comparing daytime and nighttime glare is warranted in future studies. In total, the final AIOLIS includes 37 questions: 15 questions about the frequency

Table 6. Time of Day When Symptoms Experienced before and after Surgery

| Symptom | During the Day | Dawn or Dusk | At Night |
|---|---|---|---|
| Glare | 16% (15%) | 33% (32%) | 77% (77%) |
| Blurry vision | 77% (74%) | 50% (49%) | 53% (48%) |
| Starbursts | 6% (9%) | 32% (30%) | 83% (79%) |
| Hazy vision | 65% (62%) | 48% (46%) | 38% (35%) |
| Snowballs | 9% (10%) | 31% (31%) | 81% (75%) |
| Halos | 5% (9%) | 33% (32%) | 80% (78%) |
| Floaters | 86% (89%) | 28% (43%) | 25% (39%) |
| Double images | 72% (68%) | 44% (43%) | 50% (39%) |
| Rings and spider webs | 13% (13%) | 37% (35%) | 71% (71%) |
| Flash with eyes closed | 41% (30%) | 29% (18%) | 49% (42%) |
| Distortion | 64% (60%) | 40% (47%) | 36% (44%) |
| Flash with eyes open | 43% (47%) | 36% (38%) | 39% (22%) |
| Shimmering images | 65% (46%) | 40% (17%) | 21% (25%) |
| Dark crescent-shaped shadow | 70% (61%) | 9% (36%) | 17% (24%) |

After surgery data shown within parentheses.

Table 7. Symptoms When and When Not Wearing Corrective Lenses before and after Surgery

| Symptom | Not Wearing Glasses or Contacts | Wearing Glasses or Contacts | When Wearing and Not Wearing Glasses or Contacts |
|---|---|---|---|
| Glare | 13% (57%) | 27% (8%) | 59% (35%) |
| Blurry vision | 36% (61%) | 11% (5%) | 53% (34%) |
| Starbursts | 14% (53%) | 27% (10%) | 59% (38%) |
| Hazy vision | 18% (45%) | 19% (7%) | 63% (47%) |
| Snowballs | 15% (61%) | 24% (6%) | 61% (32%) |
| Halos | 17% (60%) | 22% (6%) | 61% (34%) |
| Floaters | 16% (38%) | 13% (3%) | 71% (59%) |
| Double images | 30% (47%) | 18% (7%) | 52% (47%) |
| Rings and spider webs | 14% (65%) | 26% (9%) | 60% (26%) |
| Flash with eyes closed | 30% (60%) | 7% (7%) | 63% (33%) |
| Distortion | 18% (38%) | 29% (6%) | 53% (56%) |
| Flash with eyes open | 19% (65%) | 27% (10%) | 54% (24%) |
| Shimmering images | 17% (40%) | 24% (0%) | 60% (60%) |
| Dark crescent-shaped shadow | 23% (44%) | 27% (4%) | 50% (52%) |

Symptoms could occur only when not wearing glasses or contact lenses, only when wearing glasses or contact lenses, or when wearing and when not wearing glasses or contact lenses. After surgery data shown within parentheses.

and bother of the ocular symptoms (i.e., 30 questions), 6 general vision questions, and a question about frequency of wearing glasses or contact lenses (Appendix A, available at www.aaojournal.org). It is available on request from the American Academy of Ophthalmology for noncommercial use and is available for license for commercial use.

Other patient-reported measures of symptoms exist, but they have limitations. For example, the frequency, severity, and level of bother scales of the Quality of Vision questionnaire[10] are scored across 10 symptoms (glare, halos, starburst, hazy vision, blurred vision, distortion, double vision, fluctuation, focusing difficulties, and depth perception). The lack of differentiation of individual symptoms limits the clinical usefulness of the Quality of Vision questionnaire. In contrast, we found that the median correlation among reports of having the 14 symptoms at baseline was only 0.19, indicating that they yield substantially unique information. A recent article by Lasch et al[11] presented the Questionnaire for Visual Disturbances. The Questionnaire for Visual Disturbances is like the AIOLIS in assessing frequency, severity, and level of bother of 7 visual symptoms (starburst, halo, glare, hazy vision, blurred vision, double vision, and dark areas) using a 7-day recall interval with response options like those in the AIOLIS. However, the AIOLIS assesses several other symptoms (e.g., snowballs, rings and spider webs, and distortion). Future studies are needed to provide

Table 8. Correlations of Symptom Severity and Bother with Self-rated Vision, Satisfaction with Vision, and How Well Able to See without Corrective Lenses before Surgery

| Symptom | Poor to Excellent Vision* | Satisfaction with Vision† | Able to See without Correction‡ |
|---|---|---|---|
| Glare | −0.26 (−0.29) | −0.34 (−0.43) | −0.17 (−0.18) |
| Blurry vision | −0.39 (−0.40) | −0.43 (−0.47) | −0.24 (−0.28) |
| Starbursts | −0.18 (−0.25) | −0.25 (−0.32) | −0.16 (−0.18) |
| Hazy vision | −0.37 (−0.37) | −0.37 (−0.44) | −0.17 (−0.18) |
| Snowballs | −0.17 (−0.20) | −0.31 (−0.39) | −0.16 (−0.20) |
| Halos | −0.28 (−0.30) | −0.36 (−0.42) | −0.24 (−0.25) |
| Floaters | −0.14 (−0.22) | −0.16 (−0.29) | −0.15 (−0.24) |
| Double images | −0.16 (−0.35) | −0.22 (−0.34) | −0.23 (−0.26) |
| Rings and spider webs | −0.17 (−0.21) | −0.23 (−0.32) | −0.26 (−0.28) |
| Flash with eyes closed | −0.09 (−0.18) | −0.24 (−0.36) | −0.12 (−0.28) |
| Distortion | −0.30 (−0.25) | −0.33 (−0.42) | −0.16 (−0.15) |
| Flash with eyes open | −0.11 (−0.10) | −0.17 (−0.20) | −0.07 (−0.10) |
| Shimmering images | 0.03 (−0.29) | −0.08 (−0.46) | −0.12 (−0.34) |
| Dark crescent-shaped shadow | −0.25 (−0.39) | −0.23 (−0.23) | 0.08 (−0.28) |

Symptom bother correlations are shown within parentheses. Poor to excellent vision correlated 0.67 with satisfaction with vision and 0.40 with able to see without correction. Satisfaction with vision correlated 0.40 with able to see without correction.
*Would you say your vision now is poor, fair, good, very good, or excellent?
†How satisfied are you with your vision right now?
‡How well are you able to see now without glasses, contact lenses, a magnifier, or other corrective devices?

a head-to-head comparison of the Questionnaire for Visual Disturbances and AIOLIS.

In summary, this study provides initial support and extension information about the AIOLIS in assessing core symptoms associated with IOL implants with cataract surgery for patients who received monofocal, toric, multifocal, or extended depth of focus IOLs. The study design included extensive input from patients, clinicians, regulators, and IOL manufacturers prior to administering the survey to evaluate interrelationships between patient's symptoms, visual performance, and satisfaction under a variety of conditions. The survey asks patient to rate distance, intermediate, and near vision as well as rating symptoms during daytime, dusk, or nighttime. It also includes questions on whether and how frequently they relied on glasses or contact lenses before and after IOL surgery. The AIOLIS makes it possible for clinicians, regulators, and manufacturers to understand patients' perceptions and adaptation to a variety of contemporary IOL designs. It can also serve to provide clinicians and patients with a better understanding of the interplay between postoperative patients' symptoms, visual performance, and satisfaction.

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## Footnotes and Disclosures

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A List of Members of the Advisory Committee appears in Appendix B (available at www.aaojournal.org).

HUMAN SUBJECTS: Human subjects were included in this study. This study was approved by the UCLA Human Subjects Committee (IRB#17-000146) and the RAND Human Subjects Committee (IRB#2018-1047-AM01) and was performed in accordance with the tenets of the Declaration of Helsinki.

No animal subjects were included in this study.

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Analysis and interpretation: Hays, Tarver, Masket

Data collection: Weidmer

Obtained funding: Hays, Masket

Overall responsibility: Hays, MacRae, Holladay, Tarver, Lum, Stark, Weidmer, Kumar, Lau, Nguyen, Schallhorn, Eydelman, Masket

Abbreviations and Acronyms:
**AIOLIS** = Assessment of IntraOcular Lens Implant Symptoms; **D** = diopter; **FDA** = Food and Drug Administration; **IOL** = intraocular lens; **logMAR** = logarithm of the minimum angle of resolution.

Keywords:
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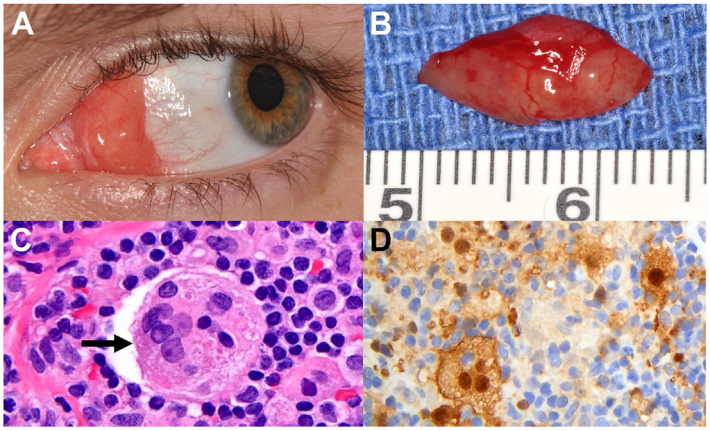
## Pictures & Perspectives




**Rosai-Dorfman Disease**

An 18-year-old man presented with a 3-month history of a rapidly growing, subconjunctival, salmon-colored lesion in the left medial palpebral aperture (**A**). Excisional biopsy removed a well-defined, gelatinous mass (**B**). Histopathology revealed lymphocytes, plasma cells and histiocytes with large, round nuclei, voluminous cytoplasm, and occasional emperipolesis (engulfment of lymphocytes) (**C**, arrow). Histiocytes demonstrated positive S100 immunostaining (**D**), confirming the diagnosis of extra-nodal Rosai-Dorfman disease. Rosai-Dorfman disease is a rare, non-Langerhans histiocytosis of unknown etiology predominantly affecting children and young adults. Unifocal disease can be treated surgically, although immunosuppressive agents are used for more extensive disease. The clinical course is typically benign (Magnified version of Figure **A**-**D** is available online at www.aaojournal.org).

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