The economic impact of blue-light filtering intraocular lenses on age-related macular degeneration associated with cataract surgery: a third-party payer’s perspective

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ABSTRACT

Objectives: Epidemiological data support an association between age-related macular degeneration (AMD) and cataract surgery that may be attributed to post-operative blue light exposure. By limiting the retina’s blue light exposure, new blue-light filtering intraocular lenses (BLF IOLs) have the potential to reduce the development of AMD following cataract surgery. In the current economic healthcare environment, there is increased interest in the cost impact of new medical technologies. The objective of this analysis was to evaluate the cost impact of a BLF IOL versus a non-BLF IOL in cataract surgery.

Methods: An economic model was developed to emulate three age-specific cohorts and to assess the clinical and economic outcomes over 5 years. Data from the published literature was supplemented with clinical expert opinion. Key literature inputs involved the risk of AMD after cataract surgery as well as laboratory and animal data on the effectiveness of the BLF IOL in reducing the risk of AMD. Clinical experts provided information on the management of AMD. Direct medical costs including the cost of the IOL, monitoring, and AMD prophylaxis and treatment were incorporated into the model. All costs were standardized to 2004 US dollars. Age-stratified sensitivity analyses were conducted.

Results: In the BLF IOL group, the 5-year age-stratified incidence of AMD ranged from 0.58 to 9.23 per 100 eyes, compared with 1.69 to 24.55 per 100 eyes in the non-BLF IOL group. The incremental cost of the BLF was offset by reduced costs associated with averted AMD treatment. Estimated savings with BLF IOLs per 100 eyes were $4,275, $29,997, and $111,734 in the 55 to 64 year-old, 65 to 74 year-old, and ≥ 75-year-old cohorts, respectively; these findings remained robust throughout the sensitivity analyses.

Conclusion: Limitations of this analysis include the lack of prospective clinical trial data that definitively demonstrate the efficacy of a BLF IOL in preventing AMD. Moreover, the efficacy data used to populate the model were derived from laboratory and animal studies. Thus, based on preliminary data, this study suggests that the economic benefits of implanting BLF IOLs during cataract surgery are observed in all patients over a 5-year timeframe although cost savings are greatest in patients ≥ 75 years.
Introduction

Age-related macular degeneration (AMD) is the leading cause of blindness in patients ≥ 60 years in industrialized countries. The prevalence of AMD is strongly age-related with some 1%, 5%, and 13% of individuals 65 to 74 years, 75 to 84 years, and ≥ 85 years, respectively, reported to have the condition. In the early stages of AMD, drusen and retinal pigmentation changes occur that may progress to the more serious geographic atrophy (GA) and exudative changes. In addition to age, AMD has been associated with cataract surgery during which the natural human lens, that has the ability to filter blue light, is extracted and replaced with a clear intraocular lens (IOL) that lacks the ability to filter blue light. Blue light has been shown to damage the retina and may increase the risk of AMD. Indeed, epidemiological data show a several fold increase in the risk of AMD after cataract surgery. Preclinical studies suggest that blue-light filtering (BLF) IOLs have a protective effect 

Moreover, a recent editorial recommended that BLF IOLs be considered to replace the natural lens during cataract surgery.

Once AMD develops, few treatments are approved and their efficacy is limited to slowing disease progression. Along with the progressive loss of vision, patients with AMD experience a profound decrease in quality of life, often relying on caregivers to assist with activities of daily living. In addition to the clinical and quality of life impact, AMD is also associated with a significant economic burden. Medical resources in managing AMD include treatments such as laser photocoagulation, verteporfin (Visudyne†), and pegaptanib (Macugen†); diagnostic tests; and physician visits.

Given the devastating effect of AMD on a patient’s life, its overall impact on society, as well as the lack of curative treatments, strategies that lower the risk of AMD have the potential to be of significant benefit. To date, only a combination of vitamins and antioxidants have been shown to decrease the risk of developing AMD. This benefit, however, is limited only to high-risk patients who experience a 25% risk reduction in developing AMD. Management of modifiable risk factors has the potential to improve clinical and quality of life outcomes and also reduce downstream healthcare costs due to the relatively expensive treatment of AMD.

A BLF lens (AcrySof Natural†) that mimics the natural human lens has recently become available in the United States (U.S.) market. The intention is to limit the exposure of the retina to blue light and subsequent damage, thereby offering the potential to reduce the development of AMD following cataract surgery. The U.S. estimated cost of this BLF IOL is approximately 1.5 times higher than the mean cost of all non-BLF IOLs. In the current environment of tighter healthcare budgets and stricter care management guidelines, third-party payers and governmental agencies are increasingly requesting information regarding the cost impact of new medical technologies prior to their adoption by these third-party payers. Therefore, the objective of this study was to evaluate the cost impact of a BLF IOL versus a non-BLF IOL in cataract surgery over a 5-year time horizon.

Methods

The economic impact of implanting a BLF IOL compared with a non-BLF IOL was assessed inpatients ≥ 55 years. This age threshold was selected as 98% of cataract surgeries are performed in this group and AMD is rare in patients < 55 years. A treatment model, developed from published literature and augmented by input from an expert panel of practicing ophthalmologists, was constructed to portray expected outcomes of the IOL options. The expert panel consisted of three individuals: (1) an anterior segment surgeon and cataract specialist; (2) a practicing retina specialist; and (3) a practicing medical and surgical retina/vitreous specialist. The three ophthalmologists reviewed and provided comments on the model approach and structure, as well as insight into the management of AMD. As the perspective of this model was that of a U.S. payer, only direct medical costs were included. Consistent with the short-term timeframe of economic models acceptable to U.S. managed care organizations, a time horizon of 5 years was used.

Model overview

A decision analytical model was developed to assess the outcomes per eye receiving one of two types of IOLs following cataract surgery (Figure 1). The model was developed in Excel 2000 (Microsoft Corporation) while TreeAge (TreeAge Software Inc.) was used to demonstrate the decision analytic structure. Outcomes were assessed for three representative cohorts of 100
eyes based on patient age at the time of cataract surgery (55 to 64 years, 65 to 74 years, and ≥75 years), with each cohort having a different 5-year risk of developing AMD. These cohorts were then assigned to either of the IOL options. The cost of cataract surgery and risk of surgical complications were considered to be the same regardless of the type of IOL implanted. Eyes could then develop AMD (geographic atrophy or exudative) or remain free of AMD during the 5-year period. While AMD would likely develop throughout the 5-year period, for the purposes of simplifying the model, AMD was assumed to develop in the middle of the 5-year period (i.e., at 2.5 years). An annual ophthalmologic visit was assumed, regardless of AMD status. Similarly, preventive therapy with vitamins and antioxidants was deemed useful for all individuals except for those <65 years without AMD unless AMD was diagnosed. Exudative AMD could be treated with laser photocoagulation, verteporfin, or pegaptanib, beginning at the time of AMD diagnosis.

Clinical model inputs

To collect the clinical model input data, a literature search was conducted in PubMed, EMBASE, and Cochrane databases to identify relevant epidemiological, clinical, and economic publications using various combinations of the following search terms: age-related macular degeneration, cataract surgery, epidemiology, treatment, pegaptanib, verteporfin, laser photocoagulation, and economics. In addition, the advisory panel reviewed and validated the model structure and approach as well as the model input data. A summary of the key clinical data is provided in Table 1. The relative risk (RR) was calculated from this odds ratio (OR) using the following formula:

$$RR = \frac{OR}{1 + I \times (OR)}$$

where $I$ is the background incidence. To assess the AMD risk that could be potentially avoided by BLF IOLs, the attributable risk due to cataract surgery was further determined by the difference in the AMD incidence between patients with and without cataract surgery. Specifically, for the patient group age ≥75 years, the background incidence of AMD was 5.40%. The relative risk of AMD following cataract surgery was 4.55 (calculated from the OR). Therefore, the overall 5-year cumulative AMD incidence rate after cataract surgery was 24.55% (i.e., 5.40% * 4.55). The attributable risk due to cataract surgery alone was then calculated (24.55% - 5.40% = 19.15%). The 80% risk reduction was applied to this attributable risk to obtain an absolute incidence rate of AMD for patients with blue-light filtering IOL:

$$19.15\% \times (1 - 0.8) + 5.4\% = 9.23\%$$
Effectiveness of BLF IOL in reducing the risk of AMD

Two pre-clinical studies support the protective effect of BLF IOLs. In a study in rabbits, one eye was implanted with a BLF IOL while the fellow eye received a non-BLF IOL, a polymethylmethacrylate (PMMA) IOL. After exposure to broad-spectrum xenon irradiation, the eye with the PMMA IOL experienced more retinal and retinal pigment epithelial (RPE) damage than the eye implanted with a BLF IOL. In another study in which human RPE cells were laden with lipofuscin fluorophore A2E, implicated as an initiator of blue-light-induced apoptosis of RPE cells, BLF IOLs decreased transmission of blue light by 50%. Furthermore, BLF IOLs reduced RPE cell death by 80% compared with cells without any lens filtration or by non-BLF IOLs. In the base case analysis, an 80% reduction in the attributable risk was, therefore, assumed. The risk reduction in AMD with BLF IOLs was then applied to the attributable risk of AMD with cataract surgery to obtain the number of AMD cases avoided by using BLF IOLs.

Economic model input

Health care resources

The model considered all AMD-related healthcare resources. Since all new AMD cases following cataract surgery were assumed to occur at the middle of the 5-year follow-up period, only resources and costs after 2.5 years were assessed for AMD management. For the first 2.5 years prior to the potential onset of AMD, healthcare resource utilization associated with AMD was considered to be the same regardless of the type of IOL received. For each resource, the corresponding Current Procedural Terminology, 4th Edition (CPT-4) codes were used to determine the associated cost.

All patients were assumed to require an initial ophthalmological visit (CPT code 92002) plus an annual follow-up visit (CPT code 92014). Among those who did not develop AMD, patients at high risk of AMD, i.e. age ≥65, were assumed to receive preventive therapy with a vitamin/antioxidant combination based on the literature and expert opinion. All AMD patients were assumed to receive this vitamin/antioxidant combination.

For patients who developed exudative AMD, conservative estimates of the cost of treatment were used so as not to over-estimate the potential economic benefit of BLF IOLs. Discussions with clinical experts and a review of the literature confirmed the absence of AMD clinical guidelines and that variation in treatment is the norm. For this model the management of AMD was restricted to treatments that are (a) available in the U.S., and (b) whose efficacy is supported by at least one randomized clinical trial. Therefore, only laser photocoagulation, verteporfin, and pegaptanib were included in the model (Table 1). As no data were available on the percentage of patients’ eligible for pegaptanib, all patients who were eligible to receive laser photocoagulation (10%) and verteporfin (25%) were assumed to receive these treatments while the balance were considered to receive pegaptanib. Fluoroscein angiography and fundus photography were assumed to be required at each visit for all exudative AMD patients (CPT codes 92235 and 92250). With verteporfin, photodynamic therapy was administered with each treatment (CPT code 67221). With pegaptanib, an additional brief visit 2–3 weeks after each drug administration (CPT code 92012) was assumed based on expert opinion. As pegaptanib is administered by intravitreal injection, the corresponding administration cost was also included (CPT code 67028). Regarding adverse events, only endophthalmitis (incidence 1.3%)
with pegaptanib resulted in resource utilization. Management of endophthalmitis included intravitreal ceftazidime and vancomycin plus a vitreous tap (CPT code 67015) and culture, and sensitivity of the vitreous fluid (CPT code 87070) that was confirmed by expert opinion. Due to the risk of endophthalmitis with the intravitreal route of administration, prophylaxis with a fourth-generation fluoroquinolone eyedrop, moxifloxacin (Vigamox, Alcon Laboratories Inc., Forth Worth, TX) was assumed based on expert opinion.

### Costs

The cost of the non-BLF IOL was $90, reflecting a weighted average cost of non-BLF IOLs. The cost of a BLF IOL was assumed to be $135, $10 more than the cost of the most expensive non-BLF IOL (i.e. currently an acrylic IOL $125). Drug costs were based on Advertised Wholesale Price or were taken from an online pharmacy. Monitoring, physician visit and administration costs, defined by CPT-4 codes, were based on 2004 Medicare reimbursement limits (Table 2). All costs were standardized to 2004 U.S. dollars.

### Analysis

The decision model was analyzed to estimate the expected costs and expected effectiveness during the 5-year follow-up period for each of the IOL options (BLF IOL vs. non-BLF IOL). Given that age is the major AMD risk factor, the model analysis was conducted for each of the three age groups. For each of the IOL groups, the total number of AMD cases per 100 eyes during the first 5-year follow-up period was estimated based on the background risk and attributable risk of AMD due to cataract surgery. Additionally, for each IOL group, total costs incurred per 100 eyes within the BLF IOL group and non-BLF IOL group during the first 5-year follow-up period were calculated comprised of the medical costs due to AMD plus the cost of the specific IOL. A discount rate of 3% was used to convert all future costs (i.e. Years 3 to 5) to the present value at the time of surgery.

The differences between the BLF IOL and non-BLF IOL groups in the AMD incidence and in the total costs per 100 eyes incurred post-cataract surgery were examined. First, it was determined whether one type of...
IOL dominated another by having both lower costs and greater effectiveness; if non-dominated, an incremental cost-effectiveness ratio of cost per AMD case avoided would be further calculated as the difference in costs divided by the difference in the AMD incidence.

Univariate and multivariate sensitivity analyses were conducted using Crystal Ball 2000, Professional Edition, version 5.2 (Decisioneering, Inc.) to identify variables that have a large influence on the results and to test the overall robustness of the analysis when the value of sensitive or clinically important or relevant variables (e.g., incidence rate of AMD, risk reduction of BLF IOL, cost of AMD treatment) were changed in the analysis. The range of values tested for each variable was determined via literature review supplemented with expert opinion.

In particular, multivariate sensitivity analyses (for example) were conducted using Crystal Ball 2000 to identify the data that contributed the most to the results and to test the overall robustness of the findings (via Tornado diagrams). The range of values tested for each variable was specified in Table 1. The influence on the results of the key variables identified from the Tornado analyses was tested via several scenario analyses.

Results

Base-case analysis

The cost associated with AMD and no AMD are shown in Figure 1. Pegaptanib was the most expensive therapy for exudative AMD, followed by verteporfin, and laser photocoagulation. The total treatment cost per AMD case, the weighted cost of treating geographic atrophy AMD and exudative AMD, was $8178. For patients who did not develop AMD, the corresponding costs were $265 for individuals aged 55 to 64 years and $590 for individuals > 65 years; the higher costs in the older cohorts were due to the use of vitamin/antioxidant combination.

The incidence of AMD increased with age regardless of IOL implanted; however, the incidence of AMD was consistently lower in the BLF IOL group compared with the non-BLF IOL group (Table 3). For eyes implanted with the BLF IOL, the 5-year incidence of AMD after cataract surgery ranged from 0.58 to 9.23 per 100 eyes, whereas a higher incidence of 1.69 to 24.55 per 100 eyes was projected for patients with non-BLF IOLs.

For all age groups, the BLF IOL cohorts were found to have lower total costs during the 5-year period compared with the non-BLF IOL cohorts (Table 3). The cost savings per 100 eyes for BLF IOLs versus non-BLF IOLs increased dramatically with age from $4275 in the 55 to 64 year-old cohort to $111734 in the ≥75-year-old cohort. Thus, the additional cost of the BLF IOL was offset by the reduced cost of managing AMD.

In the base case analyses, BLF IOLs were associated with better clinical outcomes and lower costs than non-BLF IOLs in all three cohorts. Therefore, incremental cost-effectiveness ratios were not calculated.

Sensitivity analysis

The base case results showed that the model results were sensitive to patients’ baseline AMD risk (which was affected most by age). For all three age groups, the top five most influential variables on the cost savings were identical: (1) Odds of AMD after cataract surgery, (2) AMD risk reduction by BLF IOL, (3) baseline AMD incidence, (4) pegaptanib cost, and (5) percentage of patients who develop exudative AMD. In Table 4 the five most influential variables and the corresponding change in results in the ≥75-year-old age group is shown where each variable was varied across the range listed in Table 1; this cohort was selected as these patients represent the majority of the population undergoing cataract surgery. For example, the cost-savings associated with BLF IOLs more than doubled from the base-case analysis of $111734 to $227998 when the upper limit of the 95% confidence interval of

<table>
<thead>
<tr>
<th>Variable</th>
<th>BLF IOL</th>
<th>Non-BLF IOL</th>
<th>AMD cases avoided*</th>
<th>Cost savings†</th>
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</thead>
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<tr>
<td>Age group: 55 to 64 years</td>
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<td></td>
<td></td>
<td></td>
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<tr>
<td>Incidence of AMD</td>
<td>0.58</td>
<td>1.69</td>
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<tr>
<td>Total costs</td>
<td>$44549</td>
<td>$48824</td>
<td>–</td>
<td>$4275</td>
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<tr>
<td>Age group: 65 to 74 years</td>
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<td></td>
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<td></td>
</tr>
<tr>
<td>Incidence of AMD</td>
<td>2.44</td>
<td>6.98</td>
<td>4.55</td>
<td>–</td>
</tr>
<tr>
<td>Total costs</td>
<td>$91016</td>
<td>$121013</td>
<td>–</td>
<td>$29997</td>
</tr>
<tr>
<td>Age group: ≥ 75 years</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Incidence of AMD</td>
<td>9.23</td>
<td>24.55</td>
<td>15.32</td>
<td>–</td>
</tr>
<tr>
<td>Total costs</td>
<td>$142558</td>
<td>$254292</td>
<td>–</td>
<td>$111734</td>
</tr>
</tbody>
</table>
the odds ratio of AMD after cataract surgery (i.e. 13.60 compared with 5.70 in the base-case analysis) was used.

**Discussion**

The key findings of this analysis are a reduced risk of developing AMD in the 5-year period after cataract surgery and that the additional cost of the BLF IOL is completely offset by the lower costs associated with AMD management. However, the extent of this benefit is highly dependent on the age of the patient, or more specifically, baseline risk of AMD. The 5-year incidence of AMD in patients ≥ 75 years is 5.4%; this model projected that cataract surgery increased the AMD incidence to 24.6% and that BLF IOLs reduced the incidence to 9.2%. While clinical benefits were also projected in patients < 75 years, the gains were marginal compared with those estimated in the older patient cohort. In contrast to this is a recent editorial that suggests younger patients have the most to gain from receiving BLF IOLs. As this analysis was confined to a 5-year timeframe, the potential benefits to younger patients may not have been fully demonstrated as these are likely to be realized in the longer term.

Accompanying the clinical benefits, economic benefits were also observed. Due to the reduced incidence of AMD, cost savings from avoiding AMD and its treatment of some $4000–$110 000 per 100 eyes, depending on patient age, were realized. As many patients undergo bilateral cataract surgery, the per patient savings are expected to be almost twice these estimates. Consistent with the clinical findings, the cost savings were greatest in the ≥ 75-year-old cohorts. These estimates are conservative as AMD treatment costs are likely to rise with new treatments in development, and the use of combination therapies and sequential therapy now being explored. Moreover, the model excluded other medical costs associated with AMD (e.g., falls and depression), lost productivity, and costs borne by society such as residential care; rehabilitation; housing, tax, and social security benefits. Hence, the cost savings with BLF IOLs projected in this model underestimate the full economic value of this intervention.

The theory that blue light causes damage to the retina has been shown in preclinical laboratory studies and it supports the hypothesis that BLF IOLs confer protection against AMD. It is noteworthy that blue hazard filter lights are used during argon laser treatment and in the operating room to minimize surgeon’s exposure to blue light, due to physician belief in the dangers of exposure to blue light. Definitive proof of the efficacy of BLF IOLs in reducing the risk of AMD is lacking and a long-term prospective study would be needed to fully demonstrate this benefit.

Several large prospective epidemiological studies provide strong support for the association between cataract surgery and AMD. Explanations other than blue-light-mediated damage, such as an inflammatory reaction due to the cataract surgery, a discovery bias with patients with cataracts being more likely to seek professional help, and common risk factors for the development of cataracts and AMD, have all been hypothesized to explain the association between cataract surgery and AMD, but have not been substantiated with any evidence.

Limitations of this analysis include the lack of prospective clinical trial data that definitively demonstrate the efficacy of a BLF IOL in preventing AMD. Moreover, the efficacy data used to populate the model were derived from laboratory and animal studies. We also assumed that AMD develops in the middle of the 5-year period; lack of availability of the annualized incidence of AMD following cataract surgery prohibited a more precise estimation of the effects. Due to the lack of data, an overall odds ratio of developing AMD following cataract surgery was applied to age-stratified baseline incidence rates to estimate age-specific AMD incidence in this model. However, by using the attributable risk of AMD due to cataract surgery, this potential bias in estimating the benefit of a BLF IOL may have been minimized. To examine the possible bias from the limited data sources, we performed scenario sensitivity analyses and found the model results to be consistent.

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**Table 4. Sensitivity analysis (≥ 75 years)**

<table>
<thead>
<tr>
<th>Model parameter</th>
<th>Base-case: $111 734</th>
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</thead>
<tbody>
<tr>
<td>Odds of AMD after cataract surgery</td>
<td>$35 859–$227 998</td>
</tr>
<tr>
<td>AMD risk reduction by BLF IOL</td>
<td>$24 558–$126 263</td>
</tr>
<tr>
<td>Baseline AMD incidence</td>
<td>$83 607–$135 513</td>
</tr>
<tr>
<td>Pegaptanib cost</td>
<td>$85 079–$138 388</td>
</tr>
<tr>
<td>Percentage of patients with exudative AMD</td>
<td>$110 377–$113 090</td>
</tr>
</tbody>
</table>

*AMD incidence post-cataract surgery = AMD incidence post-cataract surgery + $\text{CostB}_{\text{OIO}}$ - $\text{Cost}_{\text{BLF IOL}}$.

†$\text{CostB}_{\text{OIO}} = \text{Cost}_{\text{BLF IOL}}$.

AMD = age-related macular degeneration; BLF = blue-light filtering; IOL = intraocular lens.
within the range tested. Additionally, our model did not address the impact of multiple risk factors of AMD on the treatment cost impact other than age. Taking into account more than one risk factor may affect the results of the model. Finally, as the perspective of the analysis was that of a third-party payer, direct non-medical costs such as visual aids, and indirect costs such as patient time loss and informal care, were excluded. Our analyses and findings may be very conservative given the considerable indirect costs associated with AMD.

In the absence of viable alternative and effective treatments, leading ophthalmologists have recommended the routine use of BLF IOLs during cataract surgery. 2,27 For third-party payers, coverage of any therapy involves an assessment of the cost/benefit ratio. On the cost side, only the estimated additional cost of the BLF IOL (+$45), compared with the average cost of non-BLF IOLs, has been identified. 2 This initial cost needs to be balanced with the potential clinical and social benefits of preventing AMD in addition to the cost savings.

**Conclusion**

Based on preliminary data, the findings of this analysis suggest that the economic benefit of implanting BLF IOLs during cataract surgery will be observed in all patients over a 5-year time horizon although the greatest benefits will likely be realized in patients ≥75 years. Confirmation from prospective studies is warranted. In addition, economic analyses over a longer timeframe, i.e. a lifetime, are also needed.

**Acknowledgments**

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**References**

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