

Appendix J: Health economics

J.1 General

The economic approach to supporting decision-making for a guideline begins with a systematic search of the literature. The aim of this is to source any published economic evaluations of relevance to the topics of interest. At this stage, it may become apparent that high-quality evidence exists in the literature that exactly meets eligibility criteria for 1 or more review questions. In this circumstance, there is no need for original economic analysis for these questions. If this proves not to be the case, it may be decided that original economic modelling will be useful to inform decision-making. The aim is to produce a cost–utility analysis in order to weigh up the benefits, harms and costs of competing courses of action. The extent to which this is possible will be driven by the availability of evidence upon which to parameterise the clinical pathway and disease natural history.

J.2 Systematic review of published cost–utility analyses

J.2.1 Methods

We conducted a systematic literature search in order to identify published cost–utility analyses that may provide evidence of the cost effectiveness of the interventions in question.

Inclusion and exclusion criteria

The economic literature review aimed to identify economic evaluations in the form of cost–utility analyses exploring the costs and effects of different courses of action before, during and after phacoemulsification cataract surgery with IOL implantation. This guideline does not contain a review question on the cost effectiveness of cataract surgery per se – that is, questioning whether, for an average person with cataracts, offering cataract surgery provides good value for money compared with not offering it. It is beyond doubt that cataract surgery provide outcomes that are, on average, a good use of NHS resources. However, there is uncertainty and variability of practice regarding **to whom** surgery should be offered and **how** surgery should be planned for, undertaken, and followed up.

Search strategy

A single search was conducted to identify published cost–utility analyses of relevance to any review question(s) in the guideline. This was based on the overarching population terms from the clinical review strategies with a standard economic filter applied (see appendix D). In total, 4,306 studies were returned by the search and, after title and abstract screening, 32 full-text papers were ordered for detailed perusal, following which 2 studies were included for RQs 3&4, 1 study was included for RQ13, 1 study was included for RQ 22 and 4 were included for RQs 24 & 25

Quality appraisal

Studies that met the eligibility criteria were assessed using the quality appraisal criteria as outlined in Developing NICE guidelines (2014).

J.2.2 RQ 3: What are the indicators for referral for cataract surgery & RQ4: What are the optimal clinical thresholds in terms of severity and impairment for referral for cataract surgery**Naeim et al. (2007)**

Naeim et al. (2007) conducted an economic evaluation alongside an RCT that enrolled 250 patients with bilateral cataracts eligible for first-eye surgery in whom the predicted probability of improvement in visual function was low. The trial randomised participants to surgery or watchful waiting. The primary outcome measure was the self-reported change in visual function measured using the Activities of Daily Vision Survey (ADVS). The Health Utility Index 3 (HUI-3) instrument was also used to collect data on the HRQoL of participants at enrolment and at the 6-month post-surgery/post-enrolment endpoint.

The Cataract Surgery Index (CSI) was used to assess how likely patients were to benefit from surgery. This algorithm, which is based on expert opinion, comprises the following scoring criteria:

- for every decade over 65 years, patients receive 1 point;
- 2 points are added if there is evidence of diabetes mellitus (regardless of the presence of retinopathy);
- 1 point is subtracted if the patient has preoperative evidence of a posterior sub-capsular cataract;
- 2 points are added if there is evidence of macular degeneration;
- Preoperative ADVS (Activities of Daily Vision Score) score (range 0-100) multiplied by 0.1 is added to the total score

Patients with a CSI score of 10 points or more are considered to have a low probability (<30%) of improving with surgery.

The economic analysis was conducted from a co-payer perspective, which assumed that the costs of spectacles, medication and surgery were shared between the patient and the provider, and non-healthcare-related costs to the patient such as travelling to appointments and loss of working days were also incorporated into the analysis. Data on patients who did not undergo surgery were not included, and results are presented as simple (not incremental) cost and QALY gains for surgical intervention for the entire surgical cohort and for three scoring brackets of the CSI.

A sensitivity analysis suggests that, if costs increase by 50% or QALY gains reduce by 25%, surgery for the 'entire sample' group is not cost effective at a threshold of \$50,000 per QALY (although it should be cautioned that this was not an incremental analysis and the WTP threshold is not being applied here to incremental costs and QALYs). The analysis only considers the benefits of surgery as reported at 6 months post intervention, and therefore ignores the lifetime benefits of surgery and potential savings of low-vision and blindness costs in patients who do not have their cataracts removed. These are likely to be significant in this cohort as patients had bilateral cataract at enrolment and the condition is progressive.

Rasanen et al. (2006)

Rasanen et al. (2006) considered the HRQoL assessment of patients undergoing cataract surgery as a method of prospectively identifying those patients most likely to benefit from the procedure. Three cohorts of patients with bilateral cataract were included: 87 patients in which the first eye was to be operated (subgroup A), 73 in which both eyes were to be operated (subgroup B), and 59 patients who had a history of fellow-eye cataract removal (subgroup C). The average age (all patients) was 71 years (SD 11 years). HRQoL was measured immediately before and six months after surgery using the 15D instrument, which has a Finnish societal preference-based valuation. The analysis used a secondary care

provider payer perspective, with direct medical costs taken from a Finnish clinical patient administration database. The analysis extrapolated benefits over the average life-expectancy of each cohort, using a 5%, 3% and 1% discount rate for QALYs in scenario analyses. No consideration was given to future costs or savings. The study reported costs and QALY gains/losses for each cohort, rather than producing an incremental analysis. It is possible to calculate ICERs by comparing the costs and QALYs between the first eye only and the bilateral surgery group to create a second-eye vs unilateral surgery comparison (see table 4)

Table 1 Base case results from Rasanen et al.

| | First-eye | | Both eyes | | Incremental | | |
|--------|------------|--------|------------|--------|-------------|--------|------------|
| | Costs | QALY | Costs | QALY | Costs | QALY | ICER |
| Mean | € 1,318.00 | 0.1605 | € 2,289.00 | 0.4464 | € 971.00 | 0.2859 | € 3,396.29 |
| Median | € 1,301.00 | 0.0332 | € 2,342.00 | 0.2989 | € 1,041.00 | 0.2657 | € 3,917.95 |

The third cohort, who had a history of first eye surgery and awaiting second eye-surgery, experienced QALY losses after surgery of on average -0.0219. The reasons for this are unclear but the authors suggest that it may be due to patient characteristics: approximately two-thirds of patients in the study had good visual acuity in the eye to be operated on prior to the surgery and, of those patients who did not, the majority had good visual acuity in the fellow eye which may have had a compensatory effect and thus minimise any surgical benefit. Conversely, around one-third of patients had an additional ocular morbidity which may have contributed to their visual acuity and quality of life, and made the trade-off for second-eye surgery less likely to be beneficial. Post-surgery visual acuity data was not included in the study, making further investigation difficult. Bootstrap sensitivity analysis suggested that at a threshold of €20 000 per QALY the probability of cataract surgery being acceptable compared to a hypothetical no-surgery scenario was 51.7% in subgroup A, 59% in subgroup B and 46.4% in subgroup C.

Table 2: Economic evidence tables RQ 3 & 4

| Study, Population, Comparators, Quality | Data Sources | Other Comments | Disaggregated | | | Conclusions | Uncertainty |
|--|--|---|---------------|--------|-----------|--|---|
| | | | Cost | Effect | Cost/QALY | | |
| Naeim et al. (2007) USA Population: 250 patients eligible for first-eye surgery enrolled in an RCT Intervention: Surgery vs watchful waiting. Pre-surgical index used to assess likelihood of benefit. Partially applicable ^(a) Serious Limitations ^(b, c, d) : | Effects: Randomised controlled trial alongside economic evaluation. Costs: Co-payer perspective. Shared medical costs, also incorporated are travel and productivity costs Utilities: Activities of Daily Vision Survey (ADVS) & Health Utilities Index 3 (HUI-3). 3% discount rate | Data on patients who did not undergo surgery were not included, and results are presented as simple (not incremental) cost and QALY gains for surgical intervention for the entire surgical cohort and for three scoring brackets of the CSI. | Entire Sample | | | This study has demonstrated that a prediction rule can be used to discriminate patients for whom cataract surgery is not likely to improve outcome and for whom cataract surgery is not cost-effective. In order to develop a more precise estimate of utility gained from cataract surgery, a larger trial may be needed. | If costs increase by 50%, or QALY gains reduce by 25%, surgery for the 'entire sample' group is not cost effective at a cost-per-QALY threshold of \$50,000 |
| | | | \$1,567 | 0.041 | \$38,228 | | |
| | | | \$1,803 | 0.057 | £31,638 | | |
| | | | \$1,639 | 0.044 | \$37,250 | | |
| | | | CSI = 10 | | | | |
| | | | CSI = 11 | | | | |
| | | | CSI = >12 | | | | |
| | | | \$1,284 | 0.024 | \$53,500 | | |

a) Non-UK/NHS setting
 b) CSI "predicts" effectiveness of surgery (assumed 100% acc.). Not proven in NHS context.
 c) Time horizon of only 6 months. Ignores the lifetime benefits of surgery - preventing high scoring CSI patients from blindness, cost and utility loss in the future.
 d) Non-incremental analysis

| Study, Population, Comparators, Quality | Data Sources | Other Comments | Incremental (calculated from publication) | | | Conclusions | Uncertainty |
|---|---|---|---|--------|------------|---|--|
| | | | Cost | Effect | Cost/QALY | | |
| <p>Rasanen et al. (2006) Population: Three Finnish cohorts of patients with bilateral cataract: (A) 87 patients first eye surgery, (B) 73 bilateral simultaneous surgery, and (C) 59 with unilateral pseudophakia. The intervention was referral to a waiting list and then surgery. The comparator was a hypothetical no surgery scenario.</p> <p>Partially applicable ^a</p> <p>Serious limitations _{b,c,d}</p> | <p>Effects: Pre and-post operative utility estimates Costs: secondary care provider payer perspective Utilities: 15-D instrument immediately prior and 6-months post-surgery.</p> <p>5%, 3% and 1% discount rate for utilities.</p> | <p>The analysis extrapolated benefits over the average life-expectancy of each cohort, using a 5%, 3% and 1% discount rate for QALYs in scenario analyses. No consideration was given to visual acuity changes beyond the 6 month follow-up period. The study reported costs and QALY gains/losses for each cohort, rather than producing an incremental analysis. ICERs were generated by comparing the costs and QALYs between the first eye only and the bilateral surgery group to create a second-eye vs unilateral surgery comparison</p> | Mean €971.00 | 0.2859 | € 3,396.29 | <p>Mean utility gain after routine cataract surgery in a real-world setting was relatively small and confined mostly to patients whose both eyes were operated. The cost of cataract surgery per quality-adjusted life year gained was much higher than previously reported and associated with considerable uncertainty.</p> | <p>Bootstrap simulation showed surgery (vs none) was more costly and less effective in 46.4% of simulated cases, and more costly and more effective in 53.6% of simulated cases in subgroup A 37.9% and 62.1% in subgroup B and 51.1% and 48.9% in subgroup C.</p> <p>Bootstrap sensitivity analysis also suggested that at €20 000 per QALY the probability of cataract surgery being acceptable was 51.7% in subgroup A, 59.0% in subgroup B and 46.4% in subgroup C</p> |

| Study, Population, Comparators, Quality | Data Sources | Other Comments | Incremental (calculated from publication) | | | Conclusions | Uncertainty |
|--|--------------|----------------|---|--------|-----------|-------------|-------------|
| | | | Cost | Effect | Cost/QALY | | |
| a) Non-UK/NHS setting b) Sensitivity analysis based only on 95% CI for costs and effects (best/worst case analysis) c) 15D instrument value tariff unique to Finnish population Group C analysis indeterminate because visual loss in fellow eye since initial surgery not measured – important data to know - Likely to underestimate benefits of avoiding vision loss without longitudinal data. d) 15D may not be valid for cataract surgery: <ul style="list-style-type: none"> – Only reported dimension to improve post surgery = vision – Does not match other studies eg VFQ-25, VF-14, HUI-3 multidimensional improvements. | | | | | | | |

J.2.3 RQ 13: What is the effectiveness of laser-assisted phacoemulsification cataract surgery compared with standard ultrasound phacoemulsification cataract surgery?

Abell et al. (2014) conducted a cost–utility analysis of laser-assisted vs standard ultrasound phacoemulsification using a decision-tree model. The payer perspective was the private secondary-care provider with direct patient and Australian Medicare costs included. The model considers a hypothetical cohort of patients undergoing cataract surgery on the better-seeing eye. Utilities in the model were calculated according to a mathematical relationship between visual acuity and HRQoL proposed based on studies by Brown et al. (1999 & 2002), Lansingh et al. (2009), and Saw et al. (2005) which is given as:

$$y = -0.04792x^3 + 0.191x^2 - 0.4233x + 0.9128$$

$y = \text{utility}$

$x = \text{VA in LogMAR units}$

The authors used data on the effectiveness of phacoemulsification taken from the Swedish National Cataract Registry, a multicentre prospective trial (Hahn et al. 2010) and a large cohort study from a tertiary centre in Germany (Hoffman et al. 2011). In the absence of any equivalent evidence on laser-assisted surgery, the model assumed that the benefit of femtosecond surgery would be a 5% improvement in the number of eyes achieving ~6/12 visual acuity post-surgery. The increase in BCVA after cataract surgery in the laser group was assumed to reflect improved refraction owing to improved lens positioning as a result of more regular capsulotomy incisions, as well as a decrease in the intraoperative complication rate. Based on the simulated complication rates of standard and laser-assisted surgery and assuming visual acuity improvement of 5% in uncomplicated cases, laser-assisted surgery was associated with QALY gains of 0.06, but was also found to have increased costs, with a resulting ICER of \$AUS92,862 per QALY gained, which is above conventional thresholds of cost effectiveness. Multivariable sensitivity analyses revealed that laser-assisted surgery would need to significantly improve visual outcomes and complications rates over standard surgery, along with a reduction in cost to patient, to improve cost effectiveness. Modelling a best-case scenario of laser-assisted surgery with excellent visual outcomes (100% achieving >6/12 vision), a significant 0% complication rate and a significantly reduced total cost to the patient of \$AUS300 resulted in an ICER of \$AUS20,000 per QALY.

Table 3 Economic evidence tables RQ 13

| Study, population, comparators and quality | Data sources | Other comments | Incremental | | | Conclusions | Uncertainty |
|---|---|--|--------------|----------------|----------|--|---|
| | | | Cost (\$AUS) | Effect (QALYs) | ICER | | |
| Abell & Vote (2014) Australia. Cost-effectiveness of Femtosecond Laser-Assisted Cataract Surgery versus Phacoemulsification Cataract Surgery Partially applicable ^a Potentially serious limitations ^{b,c,d,e} | Effects: Pragmatic literature review of cataract surgery outcome and complication rates. Costs: Australian Medicare Scheme schedule fees, AMA recommendations, private health insurance company annual reports, "current industry standards". Patient payer costs included. Utilities: Based on a mathematical relationship with visual acuity | Costings are given without summary tables or justification of variability (unclear whether assumed costs). 3% discount rate used for costs only. | 928.61 | 0.01 | \$92,861 | "Even with generous assumptions for improvements in visual outcomes and reduction in complications rates over PCS, LCS fails to reach the threshold of cost effectiveness in current Australian or US dollars. A reduction in the cost of consumables and overall cost to patient increases the likelihood of LCS being cost effective." | Laser cataract surgery was considered most cost effective when 100% of patients achieved a BCVA of >6/12, cost to patient was reduced to \$300, and LCS eliminated CME, corneal decompensation, and lens dislocation completely. This resulted in an ICER of \$20 000/QALY. |

a non- UK/NHS setting (private practice in Australia)

b Base case costs are incorporated from numerous sources but the derivation of cost parameters from these sources is unclear

c Utilities are based on a mathematical relationship with visual acuity, rather than extracted from utility instruments.

d Patient payable costs for items such as glasses, which are not typically considered in the NICE reference case, are included in the model

e No PSA

J.2.4 RQ 22: What is the optimal strategy to address pre-existing regular astigmatism in people undergoing cataract surgery?

Pineda (2010) developed a decision-analytic model which examined the costs and outcomes among patients 65 years and older with cataract and pre-existing astigmatism (1.5–3.0 dioptres) who were allocated to either toric or conventional IOLs with and without intraoperative refractive correction (IRC). Data were obtained from a literature review of effectiveness studies, and a survey of ophthalmologists (n=60) conducted online in May 2008. For each treatment option, ophthalmologists indicated the percentage of patients who would normally not need visual aids for distance vision following cataract treatment. They also indicated the percentage of these patients whose uncorrected visual acuity would be 20/25 or better, worse than 20/25 to 20/40, and worse than 20/40 OU.

Surgeons also reported the percentage of patients who would require further intervention to achieve optimal distance vision and the proportion of them with less than 1.0 D and 1.0 D or more of residual refractive cylinder after cataract treatment. They also indicated the percentage of these patients who would receive nonsurgical (glasses or contact lenses) and surgical (laser vision correction, incision corneal surgery, or conductive keratoplasty) interventions for each refractive cylinder group.

The respondents reported rates of retreatment (second refractive surgery) to optimise vision, use of different re-treatment options, and the mean time between cataract and follow-up refractive surgery. In addition, the ophthalmologists indicated the percentage of their patients receiving glasses or contact lenses and undergoing refractive surgery among the 3 UCVA groups mentioned previously.

Patient utilities were based on data from a prospective study using the time trade-off and standard gamble methods among patients with various vitreoretinal diseases. Utility weights were calculated by converting the UCVA levels into Snellen decimal values (a midpoint was obtained for the level of 20/25 to 20/40 OU) and applying an equation derived by Brown et al. 2000 ($Utility = 0.37 \times UCVA + 0.514$). Each additional year after surgery was weighted by these utility values to derive quality-adjusted life years (QALYs), which were summed during 18 years and annually discounted by 3% to compute cumulative lifetime estimates.

Disaggregated and total QALYs are not reported in the text. The base-case results suggest that incremental cost differences in treatment terms are small, and that over a lifetime horizon the use of toric IOLs generates a small saving in terms of patient- and provider-borne costs. At a 77% higher toric IOL cost or at a lower spectacle independence rate (worse-case scenarios), the toric IOL became the more expensive option during the patient's lifetime. The toric IOL was not a cost-saving option across the patient's lifetime if the frequency of changing glasses was reduced to once every 3 years. The use of the toric IOL compared with the conventional IOL without IRC resulted in cost savings as long as the remaining postsurgical lifetime was at least 16½ years (for all patients) or 17 years (for patients with UCVA of 20/25 or better).

Table 4 Economic evidence table for RQ 22

| Study, Population, Comparators and Quality | Data Sources | Other Comments | Incremental costs (Lifetime) | | | Conclusions | Uncertainty |
|--|---|--|------------------------------|----------------|----------|---|---|
| | | | Cost | Effect (QALYs) | ICER | | |
| <p>Pineda et al. (2010) USA. Economic value of improved uncorrected visual acuity among patients with cataract and pre-existing astigmatism treated with toric intraocular lenses (IOLs) compared with conventional monofocal IOLs.</p> <p>Partially applicable a</p> <p>Very serious limitations b,c,d,e</p> | <p>Decision analytic model of hypothetical patients with pre-existing astigmatism. Costs and outcomes among patients 65 years and older with cataract and pre-existing astigmatism (1.5-3.0 diopters) who were receiving either toric or conventional IOLs with and without intraoperative refractive correction (IRC). Data were obtained from the literature and from a survey of 60 US ophthalmologists.</p> <p>Costs and utilities discounted at 3%</p> | <p>Lens manufacturer-authored study.</p> | £-393 | 0.06 | Dominant | <p>Toric IOLs reduce lifetime economic costs by reducing the need for glasses or contact lenses following cataract removal. These results can inform physicians and patients regarding the value of toric IOLs in the treatment of cataract and pre-existing astigmatism.</p> | <p>At a 77% higher toric IOL cost or at a lower spectacle independence rate (worse-case scenarios), the toric IOL became the more expensive option during the patient's lifetime. The toric IOL was not a cost-saving option across the patient's lifetime if the frequency of changing glasses was reduced to once every 3 years. The use of the toric IOL compared with the conventional IOL without IRC resulted in cost savings as long as the remaining postsurgical lifetime was at least 16½ years (for all patients) or 17 years (for patients with UCVA of 20/25 or better).</p> |

a non- UK/NHS setting

b inconsistent reporting of QALY gains in prose and tables (disaggregated vs incremental values)

c Utilities are based on a mathematical relationship with visual acuity, rather than extracted from utility instruments.

d Patient payable costs for items such as glasses, which are not typically considered in the NICE reference case, are included in the model

e No PSA

J.2.5 RQ 24 & RQ 25: What is the effectiveness of bilateral simultaneous (rapid sequential) cataract surgery compared with unilateral eye surgery? What is the appropriate timing of second eye surgery, taking into account issues such as refractive power after first eye surgery?

Malvankar-Mehta et al. (2013)

Malvankar-Mehta et al. (2013) developed a decision-tree model of immediate sequential compared with delayed sequential bilateral cataract surgery (ISBCS vs DSBCS). Patients in the DSBCS arm had immediate surgery on 1 eye and then the second eye within a 3-month window if they elected to undergo the second surgery. HRQoL was estimated using the patient preference values generated from visual acuity states in Brown et al. (2000). Surgery was either classified as 'successful' or as a 'failure', with failure meaning that an intra-operative or post-operative adverse event (endophthalmitis, CMO, or 'other complication') occurred. Visual acuity outcomes for endophthalmitis were based on a 1991 study of vitrectomy procedures (Doft, 1991) whereas all other success/failure rates and outcomes were taken from a single Canadian hospital. The relative effectiveness of ISBCS and DSBCS was based on expert opinion. In the base-case analysis, ISBCS dominated DSBCS (was more effective and less costly). A one-way sensitivity analysis did not change this result.

Table 5 Base-case results from Malvankar-Mehta et al. (2013)

| Treatment | Absolute | | Incremental | | |
|-----------|------------|-----------------|-------------|-----------------|----------------|
| | Costs (\$) | Effects (QALYs) | Costs (\$) | Effects (QALYs) | ICER (\$/QALY) |
| ISBCS | 1,334.08 | 0.96 | - | - | |
| DSBCS | 2,940.62 | 0.88 | 1,606.54 | -0.08 | Dominated |

Busbee et al. (2003)

Busbee et al. (2003) developed a decision-tree-based cost-utility analysis of second-eye surgery based on data from the Patients Outcomes Research Team (PORT) study in the USA, which included 722 participants (mean age 72yrs) undergoing cataract extraction surgery. The comparator was unilateral pseudophakia, and costs and QALY gains were considered over a life expectancy time horizon. The model included costs for cataract surgery, ambulatory and surgical procedures and retinal procedures. It also included drug expenditure costs associated with cataract surgery for medical and post-operative management. The cost of cataract surgery and management of endophthalmitis, intraocular lens dislocation, cystoid macular oedema and lost lens fragments was assumed to occur close to the initiation of cataract management whereas posterior capsule opacification (PCO) and retinal detachment incurred costs at the mean time of treatment after surgery. No cost information was included for unilateral pseudophakia, and the model assumed that the post-operative visual acuity in the second eye was equal to that of the first-eye surgery. Second-eye cataract surgery resulted in a gain of 0.92 quality-adjusted life-years (QALYs) over 12 years (discounted at 3% per annum). Second-eye cataract surgery resulted in a total discounted health-care cost of US\$2,509, giving an estimated cost-utility of second-eye cataract surgery of US\$2,727 per QALY gained. No incremental analysis was conducted.

Sach et al. (2010)

Sach et al. (2010) conducted a cost-utility analysis as part of a trial of second-eye cataract surgery (Foss et al, 2006). The cohort was women over 70 years of age with a history of

successful cataract surgery and an operable cataract in the absence of other ocular comorbidities. The comparison was patients on a watchful waiting list. HRQoL was measured using the EQ-5D, and the payer perspective was NHS and PSS with carer costs included in an additional scenario analysis. The mean total cost per patient for the lifetime analysis was £12,171 and £10,887 in the operated and the control group, respectively. The incremental cost-effectiveness ratio (ICER) for surgery in the base case was £17,299 per QALY gained. The authors discuss the limitations of the EQ-5D for detecting both the quality of life of patients with a cataract prior to surgery and the gain in HRQoL incurred through surgery, highlighting this as a possible reason for their comparatively high ICERs relative to other studies.

Frampton et al. (2014)

Frampton et al. (2014) developed a cost–utility model based on a systematic review of the clinical effectiveness and cost effectiveness of second-eye cataract surgery. They identified 3 randomised controlled trials (RCTs) of clinical effectiveness, 3 studies of cost effectiveness and 10 studies of health-related quality of life which met their inclusion criteria and, where possible, were used to inform their economic analysis. Studies did not provide evidence that second-eye surgery significantly affected HRQoL, apart from an improvement in the mental health component of HRQoL as measured by the HUI (Health Utility Index -3) in 1 RCT. The health economic analysis was conducted from the NHS and PSS perspective. It simulated a cohort of patients undergoing either second-eye surgery or continued as unilateral pseudophakia cases. In the surgery arm, people underwent successful surgery or had an intra-operative or late complication (endophthalmitis, retinal detachment, PCO, cystoid macular oedema (CMO), lost-lens fragments; with risks for PCO and retinal detachment modelled time-dependently on a lifetime and 3-year time horizon respectively). Utility losses and costs for adverse events were applied for 1 year, with costs and QALYs discounted at 3.5% per annum. Second-eye surgery generated 0.68 incremental QALYs with an ICER of £1,964. Model results were most sensitive to changes in the utility gain associated with second-eye surgery, but the procedure remained well below conventional limits at £5,734/QALY even when a utility gain of as low as 0.02 was modelled. The model was otherwise robust to changes in parameter values. The probability that second-eye surgery is cost-effective at willingness-to-pay thresholds of £10,000 and £20,000 was 100%.

Table 6 Base-case results from Frampton et al. (2014)

| Treatment | Absolute | | Incremental | | |
|-----------------------|-----------|-----------------|-------------|-----------------|---------------|
| | Costs (£) | Effects (QALYs) | Costs (£) | Effects (QALYs) | ICER (£/QALY) |
| No second-eye surgery | 411 | 5.29 | - | - | - |
| Second eye surgery | 1,752 | 5.97 | 1,341 | 0.68 | 1,964 |

Table 7 Economic evidence tables RQs 24 & 25

| Study, Population, Comparators, Quality | Data Sources | Other Comments | Disaggregated | | | Conclusions | Uncertainty |
|---|--|--|---------------|----------------|---------------|--|--|
| | | | Cost | Effect (QALYs) | Cost per QALY | | |
| <p>Busbee et.al 2003 “Cost-utility analysis of cataract surgery in the second eye”. 722 US patients (72yrs) undergoing cataract extraction in the PORT study. Comparator: Unilateral surgery (non-incremental) Partially applicable^a Very serious limitations^{b,c,d,e,f}</p> | <p>Effects: Assumed that the second eye VA would be equal to that of the first-operated eye. Costs: Direct surgical costs of second eye surgery (zero costs for first-eye). Retinal procedures, drug expenditure for medical & post-operative management. Medicare 2001 outpatient fee-schedule. Utilities: Based on a mathematical relationship with VA. 3% discount rate.</p> | <p>Reports cost-effectiveness ratio, not ICER.</p> | \$2,509 | 0.92 | \$2,727 | <p>“Second-eye cataract surgery resulted in a total discounted health-care cost of US\$2,509, giving an estimated cost–utility of second-eye cataract surgery of US\$2,727 per QALY”</p> | <p>A one-way sensitivity analysis was performed in which the utility values, costs and discount rates were varied within a +/- 25% range. This had little impact on the overall results.</p> |

a non- UK/NHS setting

b Base case costs are incorporated from numerous sources but the derivation of cost parameters from these sources is unclear

c Utilities are based on a mathematical relationship with visual acuity, rather than extracted from utility instruments.

d Patient payable costs for items such as glasses, which are not typically considered in the NICE reference case, are included in the model

e No PSA

f No incremental analysis

| Study, Population, Comparators, Quality | Data Sources | Other Comments | Incremental | | | Conclusions | Uncertainty |
|---|---|--------------------------------------|-------------|--------|--|--|--|
| | | | Cost | Effect | Cost/QALY | | |
| <p>Sach et.al 2010 UK study. Second-eye cataract surgery in elderly women: a cost-utility analysis conducted alongside a randomized controlled trial” 229 (116 int. 113 ctrl). IBSCS vs 12 month waiting Directly applicable</p> <p>Potentially serious limitations ^{a,b,c}</p> | <p>Effects: EQ-5D in trial. Assumed that the utility difference between operated and unoperated eyes remains constant until death</p> <p>Costs: contacts with health and social services, care home admissions, informal care, equipment, and home modifications. Patient diaries. Deterministic.</p> <p>Utilities: In trial. EQ-5D at baseline & 6 months. Effect difference assumed constant over lifetime. 3.5% discount rate. For costs and utilities.</p> | Used a WTP threshold of £30,000 QALY | £646 | 0.015 | <p>1-year time horizon: 44,263 (no carer costs) 58,667 (costs of carer time included)</p> <p>Lifetime horizon: 17,299 (no carer costs) & 41,973 (carer costs included)</p> | “Second-eye cataract surgery is unlikely to be cost-effective in the short term, but provides greater value for money in the long term, compared with no second – eye surgery” | The threshold analysis showed that the cost of the cataract operation had to be reduced to 68% of its actual cost for the incremental cost per QALY to be below the threshold of £30,000 per QALY, if a 1yr time horizon was used. |
| <p>a Deterministic cost parameters b Uses the upper limit of the NICE decision threshold for cost-effectiveness. c. Includes some wider background (including independent sector) costs in the base-case analysis that would be better expressed in a sensitivity analysis c No PSA</p> | | | | | | | |

| Study, Population, Comparators, Quality | Data Sources | Other Comments | Incremental vs no second-eye surgery | | | Conclusions | Uncertainty |
|---|--|--|--------------------------------------|--------|--------|---|---|
| | | | Cost | Effect | ICER | | |
| <p>Frampton et al. (2014) Simulated UK cohort of adults with cataract eligible for second eye surgery vs a hypothetical no surgery arm.</p> <p>Directly applicable.</p> <p>Minor Limitations (a, b).</p> | <p>Effects: Systematic review of randomised controlled trials and economic evaluations. Costs: NHS Reference Costs 2011-12, PSSRU costs 2012, other economic evaluations. NHS/PSS perspective. Utilities: Taken from systematic review and based on Japanese ECCERT (2011) cohort study.</p> | <p>The model assumes that patients undergoing surgery experience either uncomplicated surgery or experience a short-term or long term complication: PCO, retinal detachment, endophthalmitis, lost-lens fragments & CMO are modelled.</p> <p>3.5% discount rate for costs and utilities.</p> | £1,341 | 0.68 | £1,964 | <p>“Second-eye cataract surgery is generally cost-effective based on the best available data and under most assumptions. However, more up-to-date data are needed. A well-conducted RCT that reflects current populations and enables the estimation of health state utility values would be appropriate. Guidance is required on which vision-related, patient-reported outcomes are suitable for assessing effects of cataract surgery in the NHS and how these measures should be interpreted clinically.”</p> | <p>Model results were most sensitive to changes in the utility gain associated with second-eye surgery, but otherwise robust to changes in parameter values. The probability that second-eye surgery is cost-effective at willingness-to-pay thresholds of £10,000 and £20,000 is 100%.</p> |
| <p>a) Clinical effectiveness studies were all conducted more than 9 years ago. For some vision-related patient-reported outcomes and HRQoL measures, thresholds for determining important clinical effects are either unclear or have not been determined.</p> <p>b) Patients had good vision pre surgery which may not represent all patients eligible for second-eye surgery.</p> | | | | | | | |

J.3 Original cost–utility model – methods

J.3.1 Decision problem

Table 8: Research questions

| | |
|------------|--|
| RQ3 | What are the indicators for referral for cataract surgery |
| RQ4 | What are the optimal clinical thresholds in terms of severity and impairment for referral for cataract surgery |

The guideline committee prioritised these review questions for original health economic modelling. The evidence obtained from published economic evaluations (J.2.2) was not sufficient to provide guidance to answer the review questions. The guideline committee reviewed this evidence and emphasised that determining the probability of a poor outcome in cataract surgery involves the weighing of numerous risks, with some complications interacting to increase the likelihood of future complications. Although the studies presented here attempted to address this in a limited sense, they used tools that are not widely validated or directly applicable in an NHS context and relied heavily on expert opinion for parameterisation. For these reasons the committee agreed that an original analysis was required.

The guideline committee discussed early in the process of guideline development that there are varying commissioning criteria depending on geographic locality which have introduced variation in access to cataract surgery. There is an ongoing debate as to whether prioritisation algorithms are needed to ration cataract surgery in order to maximise value for money. A central point of contention in these proposals is the incorporation of visual acuity thresholds to define the population eligible for cataract surgery. This issue is contentious because there is a lack of evidence that measured visual acuity accurately reflects the morbidity and quality of life implications of cataract. Visual acuity as measured using Snellen or logMAR cannot directly account for symptoms such as glare, doubling of vision, diminished contrast sensitivity, changing colour perception and other factors which, according to the guideline committee, may significantly affect people's quality of life before visual acuity declines to a given threshold value. However, there is some uncertainty about the trade-offs in benefits, harms and costs of cataract surgery in patients who have good vision, and particularly in patients with good vision but comorbidities or ocular characteristics which increase their risks of poor visual outcome and requirement for further procedures. The difficulty in measuring the morbidity caused by cataract means that creating a generalised estimate of the efficacy of surgery is challenging. Simple measures of visual acuity are argued to be deficient by many ophthalmologists for this purpose, and generic measures of health-related quality of life (HRQoL) which can be used to generate QALY estimates may lack the sensitivity to detect the impact of cataract symptoms such as glare, or altered colour perception. The guideline committee expressed an interest in developing a health economic model that could establish estimates of how effective in terms of QALY gains cataract surgery needs to be given a wide range of patient risk factors for poor outcome, in order to be considered cost effective.

Table 9: PICO

| | |
|---------------------|--|
| Population | Adults with symptomatic cataract <ul style="list-style-type: none"> • In a first eye (the fellow eye being symptomatically unaffected) • In both eyes • In a second eye (the fellow eye being pseudophakic) |
| Intervention | Phacoemulsification cataract surgery with IOL implantation |
| Comparators | <ul style="list-style-type: none"> • No surgery • Delayed surgery |

| | |
|-----------------|---|
| Outcomes | A cost–utility analysis was constructed based on the quality of life (in quality-adjusted life-years [QALYs]) and costs |
|-----------------|---|

Two separate decision problems were explored:

- people with no history of cataract surgery but at least one symptomatic cataract (first-eye surgery); in a proportion of these cases bilaterally symptomatic cataracts are present
- people with 1 pseudophakic eye and 1 eye with a symptomatic cataract. (second-eye surgery)

J.3.2 Overview of the model

An Excel model was developed that compares 3 strategies: no surgery, immediate surgery, and delaying surgery until VA reaches a specified threshold. The delayed surgery arm allows for the simulation of different visual acuity (VA) thresholds so that the impact on cataract surgery cost effectiveness can be examined. The model differentiates between first and second operated eyes, incorporates visual acuity changes over time in eyes both pre- and post-operatively, and includes risk factors which influence the visual acuity outcome of surgery. The model includes the cost of surgery including outpatient care, explicit costs of measures to treat and monitor endophthalmitis, posterior capsular opacification (PCO) posterior capsular rupture (PCR) and retinal detachment, and the NHS and PSS costs of support services for people with low vision.

This model represents a departure from the typical decision models developed in NICE Clinical Guidelines. Most health economic analyses aim, based on the average effect of an intervention in a cohort, to establish whether its benefits and harms justify the costs when these are averaged out over the population. In this analysis, it was necessary to move away from this assumed average approach into building a model which might identify the particular characteristics of people with cataracts that can change the expected balance between benefits, harms and costs. This approach – which may be compared to an extreme form of subgroup analysis, in which infinitely many subgroups are possible – also necessitated moving away from the normal practice of estimating a mean effect that represents how different interventions change people's quality of life. It is usual practice for models to be developed based on clinical evidence of effectiveness (derived, ideally, from randomised controlled trials of the interventions) but, in this case, an average effect would not be appropriate. In any case, there was no review question in this guideline on the effectiveness of cataract surgery compared with none (and the trials that would be necessary in order to meet such a question cannot ethically be conducted). The model takes into account the available evidence on multiple risk factors and other patient characteristics and generates an estimate of the minimum magnitude of change in HRQoL that would be required to make cataract surgery cost effective, for a person – or a population of people – with specified characteristics. Therefore, the model is not designed to generate ICERs that suggest whether surgery is or is not cost effective.

J.3.2.1 Modelled populations and interventions

The guideline committee advised that, from a purely pathological point of view, the modelled population should be assumed to have bilateral cataracts (except in the case of unilateral pseudophakia). However, it emphasised that this is not necessarily the same thing as bilateral **symptomatic** cataracts; rather, it is the case that a cataract can always be detected in the fellow eye of anyone with at least one symptomatic cataract.

Phacoemulsification cataract surgery involves the use of an ultrasonic probe to break up the lens which is then aspirated from the eye and replaced with an intra-ocular lens (IOL) implant. It is by far the most preferred technique for cataract removal, and the most commonly performed surgical procedure in the NHS. The most recently published (2014–15) Hospital Episodes Statistics (HES) data show that there were 367,267 finished consultant

episodes with the HRG code BZ02Z - 'Phacoemulsification cataract extraction and lens implant' (NHS Digital, 2017) in England and Wales. It is notable that the NHS Reference Costs report 291,133 for the same period – 76,134 fewer over the same period. We have been unable to ascertain the reason for this disparity.

We based our modelled cohort on the large Royal College of Ophthalmologists' National Ophthalmology Database (RCOphth NOD) study of cataract surgery. The database was established to provide national audit and research data, and to provide an evidence base for revalidation standards allowing ophthalmologists to compare their surgical outcomes with those of their anonymised peers. The RCOphth NOD is the formalised successor to the ad hoc collaboration that resulted in the Cataract National Dataset publications. The RCOphth NOD covers a range of conditions and operations, and collates pseudo-anonymised data collected during routine clinical care using the Electronic Medical Records (EMR) system. The most recent, peer-reviewed publication from the RCOphth NOD on the outcomes of cataract surgery (Day et. al 2015) details 180,114 cataract operations performed on 127,685 patients eligible for analysis. These were performed by 995 surgeons at 27 NHS Trusts in England and 1 in Scotland. Median patient age at first-eye cataract surgery was 77.1 years (IQR: 69.7–82.8); and 51,838 (40.6%) patients were male.

The model uses a patient perspective for outcomes and an NHS and PSS perspective for costs, in line with *Developing NICE guidelines* (2014).

J.3.2.2 Model structure – general

We built a model with a 3-month cycle length and lifetime horizon, with costs and benefits discounted at 3.5% per annum. The structure allows for the simulation of time-dependent decline in visual acuity in the pre-surgical states, and also the change in visual acuity following surgery. We model the decline in visual acuity associated with delayed surgery according to natural history data discussed in section J.3.3.5. We derive transition probabilities from the 'surgery' event' to the visual outcome states using data from the RCOphth NOD (see J.3.3.2). We assume that endophthalmitis, posterior capsule opacification (PCO) and retinal detachment occur at fixed rates and incur additional costs, but are not modelled as separate states as they are typically resolved within the timeframe of a single cycle. We model the HRQoL impact of endophthalmitis, in addition. PCR is tracked post surgically as this is the most significant modifier of short-term outcome identified in the RCOphth NOD, has additional cost implications and also increases the risk of short- and long-term such adverse events as endophthalmitis and retinal detachment.

We recognise that cataract surgery has other side-effects, we assume that these tend not to be predictable and are either extremely rare or do not typically have long-term implications for HRQoL or visual function. Therefore, we assume that their costs are included in the average reference cost for surgery. Within each state of the model, mortality occurs as per probabilities derived from Office for National Statistics lifetables (2013–2015), with an additional mortality risk associated with low visual acuity.

Model states are defined in Table 10. Note that a 'good visual outcome' does not necessarily imply that there is no probability of visual deterioration in that eye for the rest of the patient's life; it is simply a way of classifying the immediate effect of the operation.

Table 10: Modelled health states

| Health States | |
|-----------------------------|--|
| Asymptomatic cataract | A state in which a cataract is present, but does not present symptomatically |
| Symptomatic cataract | A state in which a cataract is present and symptomatic, but the simulated patient is not currently listed for surgery. Patients remain in this state until death when 'no surgery' is simulated and, in the 'delayed surgery' arm, remain in the state until VA meets a given threshold. |
| Symptomatic on waiting list | This state reflects the period between referral for surgery and surgery. Dwell-time is a function of length of waiting list, which may be varied. |
| No visual loss -PCR | A post-surgical state associated with good visual outcome and no occurrence of intraoperative PCR. |
| No visual loss +PCR | A post-surgical state associated with good visual outcome but with a history of intraoperative PCR |
| Visual loss -PCR | A post-surgical state associated with a doubling or worse of the pre-surgical visual angle, without PCR |
| Visual loss +PCR | A post-surgical state associated with a doubling or worse of the pre-surgical visual angle, with PCR |
| Death | All-cause mortality |

Figure 1 provides a schematic depiction of the generic model structure, showing all possible states, entry points and transitions. Depending on the decision problem and strategy simulated, only some of these will be possible, as depicted in subsequent figures.

It may be noted that, for 'eye 1', the 'asymptomatic cataract' state is not possible. It is a fundamental assumption of this model that people under consideration for surgery must have a cataract which is affecting them in at least 1 of their eyes.

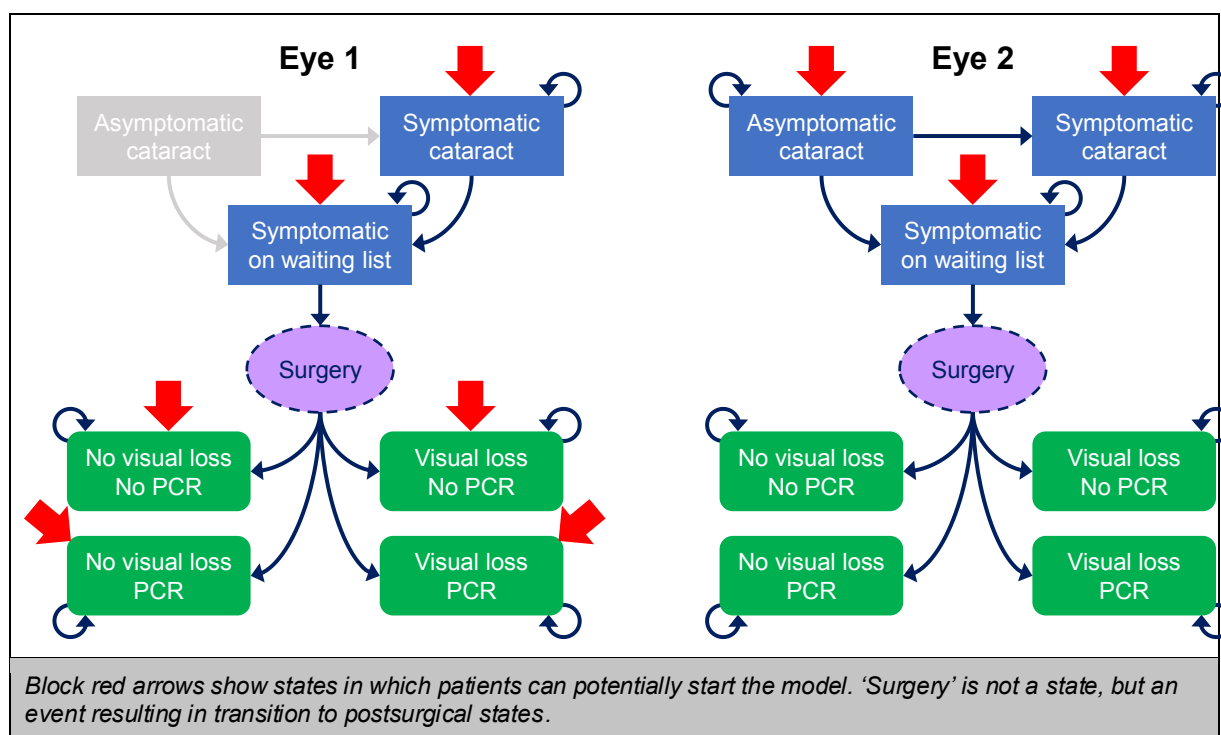


Figure 1: Overall structure of original cost-utility model

J.3.2.3 Model structure – first-eye surgery

Figure 2 depicts how the general model structure is deployed in the 3 strategies simulated for the first-eye surgery decision problem.

- In the case of **immediate surgery**, everyone joins the waiting list for first-eye surgery from the outset. The second eye of these people may be symptomatic (in which case it will also be assigned to the 'waiting list' state, and will receive surgery in the same 3-month cycle as the first eye or asymptomatic (in which case, it is subject to a probability of developing symptoms as the model progresses).
- In the case of **delayed surgery**, the case will be identical to immediate surgery for anyone presenting with both eyes at or below the acuity threshold determining access. However, if one or both eyes have acuity better than the threshold, they will remain in the 'symptomatic cataract' state until their sight deteriorates to the required degree, at which point they will join the waiting list for surgery. For the second eye, transition from 'asymptomatic cataract' directly to the waiting list is possible if the level of acuity impairment in the eye had already crossed the threshold before the cataract became symptomatic.
- In the case of **no surgery**, the first eye always remains symptomatic until death. The second eye may start as symptomatic or develop symptoms over time; in either event, as with the first eye, it remains symptomatic until death.

J.3.2.4 Model structure – second-eye surgery

The model structure for second-eye surgery is similar, with some slight modifications. It is shown in Figure 3. Regardless of strategy, the first-eye in the second-eye surgery arm is assumed to be pseudophakic, that is – the first-eye has had a cataract successfully removed and an IOL implanted. We assume that the visual acuity of this pseudophakic first eye represents a weighted average of possible outcomes from the initial surgery, with probabilities of each assumed to reflect the average observed across the population. No subsequent transitions are modelled for the first eye, but the model does track the visual acuity changes of the pseudophakic first eye over the remainder of life-expectancy as described in section J.3.3.5. Additionally, the 'asymptomatic cataract' state is no longer possible for the second eye, as this decision problem envisages people in whom second-eye surgery is being considered, who must therefore have some degree of cataract-related impairment in the eye in question.

- In the case of **immediate surgery**, everyone joins the waiting list for second-eye surgery from the outset.
- In the case of **delayed surgery**, second eyes which meet the acuity threshold will also join the waiting list immediately. However, eyes that have acuity better than the threshold will remain in the 'symptomatic cataract' state until their sight deteriorates to the required degree, at which point they will join the waiting list.
- In the case of **no surgery**, no transitions occur: the first eye remains in its assigned postsurgical category and the second eye remains symptomatic until death.

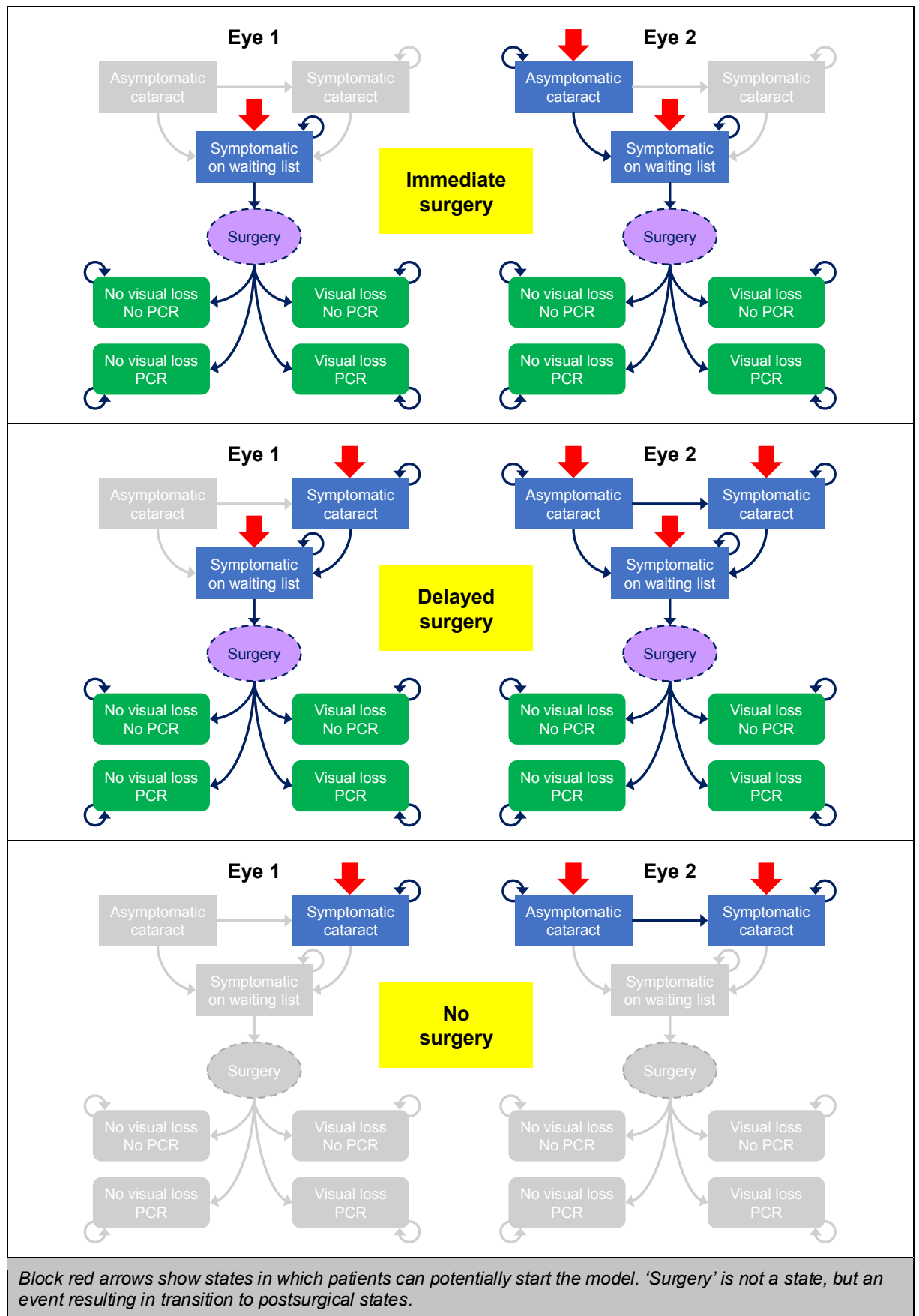


Figure 2: Structure of original cost-utility model – first-eye surgery (3 strategies modelled)

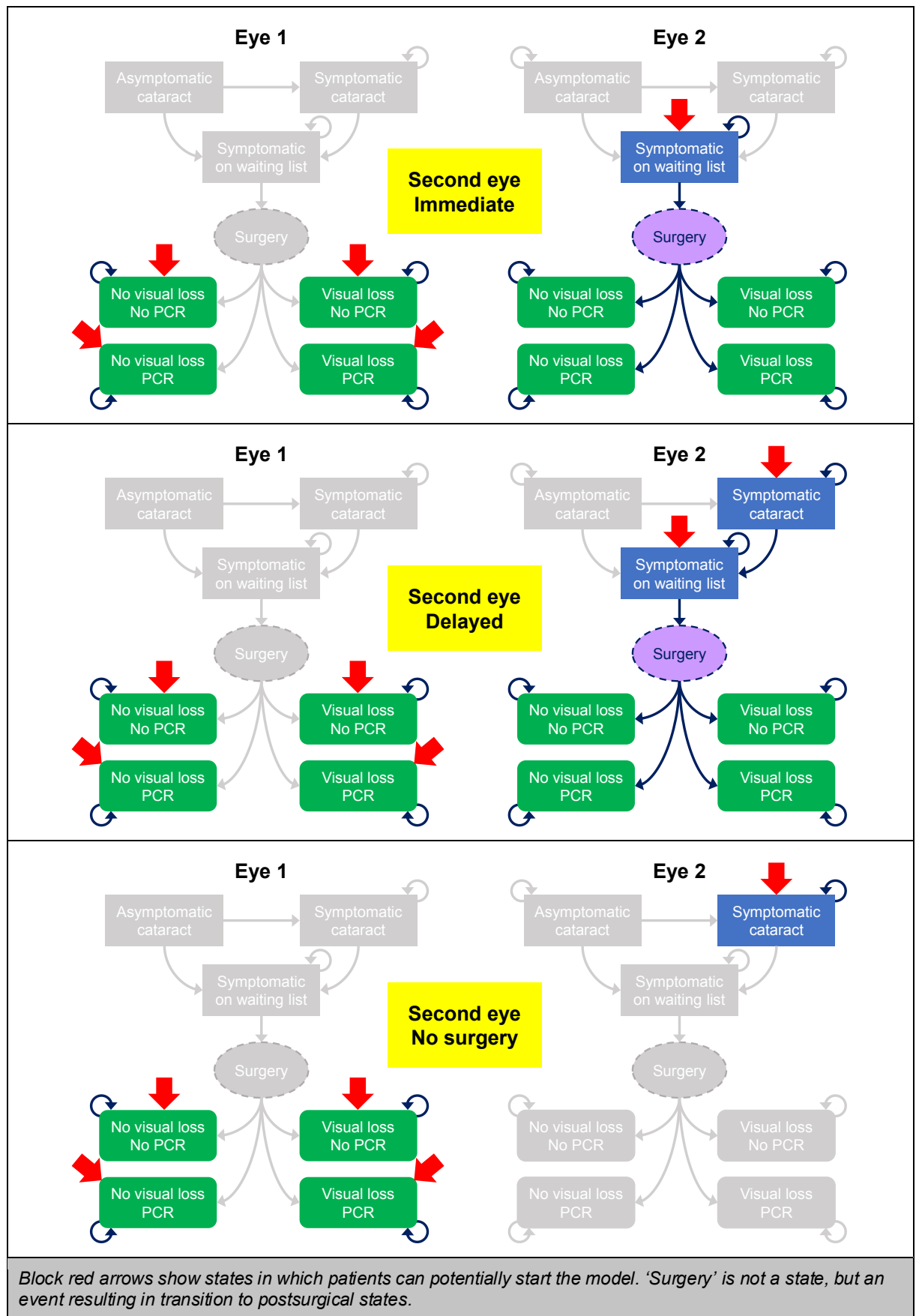


Figure 3: Structure of original cost-utility model – second-eye surgery (3 strategies modelled)

J.3.2.5 Key assumptions

There are a number of assumptions built into the economic model which need to be considered when analysing the results generated. These are summarised in Table 11.

Table 11: Key assumptions of original cost–utility model

| |
|--|
| <p>Interventions</p> <ul style="list-style-type: none"> • The model considers phacoemulsification cataract surgery only <ul style="list-style-type: none"> ◦ It is uncommon, but some cataract operations are performed using small incision surgery. We assume that this is sufficiently rare as to not incur costs that would not be captured by the mean costs of phacoemulsification. In cases where conversion from phacoemulsification cataract surgery is required, any additional costs are reflected in the standard reference cost used. ◦ It is not possible, owing to a lack of evidence, to differentiate the visual outcomes of patients who require conversion so it is assumed that the relevant proportions are reflected in the RCOphth NOD. • We assume that the NHS Reference cost of phacoemulsification cataract surgery incorporates the costs of perioperative adverse events such as transient raised intraocular pressure which are treated within the same episode of care. These events are therefore not modelled separately. • We assume that the NHS Reference Costs for cataract surgery likewise incorporate the range of lens types that are typically used and therefore exclude any additional unit costs for lenses to avoid potential double counting. Similarly it is assumed that the costs of more complex cases that require general anaesthesia or additional medications as part of their surgical episode are accounted for in the higher bands of CC codes in the reference costs. <p>Natural history</p> <ul style="list-style-type: none"> • The rate of visual acuity decline on waiting lists is inferred from very limited data. The natural history of cataract, in terms of long-term visual acuity impact, is poorly described in the literature. Data used should be regarded as speculative estimates of the true rate of VA decline over time and regarded with appropriate caution. • We assume that all patients present with some degree of bilateral cataract, based on the committee advice that a detectable, operable cataract in a single eye is a strong predictor of there being a detectable, operable cataract in the fellow eye which typically presents at a similar rate to the first eye. However, we do not assume that the cataracts in both eyes have a symptomatic impact. • We assume that the visual acuity of patients who experience a good outcome can be predicted as a linear function of their preoperative visual acuity as detailed in the RCOphth NOD. For patients who experience a poor visual outcome, we derive probabilities from the categorical changes in LogMAR VA pre- to post-operatively as detailed in the RCOphth NOD <p>Long-term effects</p> <ul style="list-style-type: none"> • Visual acuity decline after cataract surgery is based on a single study from Sweden with a 15-year follow-up period. No equivalent study from an NHS setting was available. • We do not model the complex interaction of adverse events beyond the increased risks of retinal detachment and endophthalmitis associated with PCR. Likewise, we do not consider the increased risk of events such as retinal detachment after vitrectomy to treat endophthalmitis, or following Nd:YAG Laser capsulotomy to treat PCO. This is because a) the committee regarded such events as occurring in a small sub-population of the already small number of patients who experience any adverse events from cataract removal, and this the additional complexity was unlikely to significantly alter the conclusions of the model and b) there was very limited evidence to parameterise a more complex model of such interactions. <p>Utilities</p> <ul style="list-style-type: none"> • We acknowledge that HRQoL in people with cataract is defined by more than visual acuity alone. This is why we do not make any assumption about the level of HRQoL benefit that surgery confers. However, in modelling the longitudinal natural history of (operated and unoperated) cataract, we assume that the magnitude of change in HRQoL over time is proportional to the magnitude of change that is predicted by changes in visual acuity alone. • We model the QALY decrement associated with the chronic impact of endophthalmitis, which probably reflects the degree of lasting visual impairment experienced by cases. The acute impact of endophthalmitis such as pain and temporary loss of VA are not captured by our model beyond |
|--|

any impact the recollection of such events might have on patients scoring of EQ-5D domains 1 year after infection.

- We do not model disutility for other adverse events such as PCR or PCO, owing to a lack of evidence that might provide reasonable estimates of disutility or the duration of health loss associated with these events. Where PCO is concerned, we assume that some proportion of the impact is captured by the slow deterioration of acuity over time in pseudophakic eyes, which has HRQoL impacts, in our model.

J.3.3 Parameters

Identifying sources of parameters

Clinical reviews are, in most cases, the primary source of evidence for NICE economic models. As discussed in section A.2.3.1 there was no evidence in the clinical reviews for RQs 3 and 4 which could be implemented in this health economic analysis. Parameters were therefore identified through informal searches that aimed to satisfy the principle of ‘saturation’ (that is, to ‘identify the breadth of information needs relevant to a model and sufficient information such that further efforts to identify more information would add nothing to the analysis’ [Kaltenthaler et al., 2011]). We conducted searches in a variety of general databases, including Medline (via PubMed), the Cochrane Database of Systematic Reviews and GoogleScholar.

When searching for quality of life, resource use and cost parameters in particular searches were conducted in specific databases designed for this purpose, the CEA (Cost-Effectiveness Analysis) Registry and the NHS Economic Evaluation Database (NHS EED) for example.

We asked the guideline committee to identify papers of relevance. We reviewed the sources of parameters used in the published CUAs identified in our systematic review (see J.2, above); during the review, we also retrieved articles that did not meet the formal inclusion criteria, but appeared to be promising sources of evidence for our model. We studied the reference lists of articles retrieved through any of these approaches to identify any further publications of interest.

In cases where there was paucity of published literature for values essential to parameterise key aspects of the model, data were obtained from unpublished sources; further details are provided below.

Selecting parameters

Our overriding selection criteria were as follows:

- The selected studies should report outcomes that correspond as closely as possible to the health states and events simulated in the model.
- The selected studies should report a population that closely matches the UK population (ideally, they should be drawn from the UK population).
- All other things being equal, more powerful studies (based on sample size and/or number of events) were preferred.
- Where there was no reason to discriminate between multiple possible sources for a given parameter, we gave consideration to quantitative synthesis (meta-analysis), to provide a single summary estimate.

J.3.3.1 General

Epidemiological parameters were obtained via a literature review of published studies and exploring available national statistics and health outcome databases.

Perioperative complications of cataract surgery that increase relative costs and harms are rare. The principal source of epidemiological information on these complications in England is the National Ophthalmology Database, which incorporates the National Cataract Dataset and details 75,827 operations performed in 34 participating centres across the NHS in its most recently published audit (Day et al. 2016). The data include visual outcomes, the status of the eye (first/second eye surgery), baseline patient characteristics, comorbidities and peri/post-operative complications.

J.3.3.2 Visual outcomes of cataract surgery

The RCOphth NOD provides data on baseline and postoperative visual acuity such that a state-transition model could be built with individual states pertaining to Snellen/logMAR ranges. However, this is impractical computationally as it increases the number of states needed to incorporate memory into the model and provides little benefit to decision makers, since costs and QALYs cannot be reliably attributed with available data to those VA state transitions. Instead, we consider the dichotomous outcomes of “good” and “poor” visual outcomes as defined by Sparrow et al. (2012) and Day et al. (2015) (where a poor outcome is a doubling or worse of the visual angle, pre- to post-operatively – for example 6/12 – ≥ 6/24).

Table 12 Matrix of baseline and post-operative visual acuity from Day et al. (2015)

| | | VA at surgery | | | | | |
|--------------------------|------------|---------------|------------|------------|------------|------------|-------|
| | | >1.20 | >0.90-1.20 | >0.60-0.90 | >0.30-0.60 | >0.00-0.30 | ≤0.00 |
| VA 4 months post-surgery | ≤0.00 | 2,591 | 2,406 | 8,981 | 17,921 | 8,259 | 2,367 |
| | >0.00-0.30 | 2,373 | 2,070 | 8,709 | 16,567 | 5,227 | 572 |
| | >0.30-0.60 | 1,225 | 873 | 3,949 | 5,033 | 812 | 89 |
| | >0.60-0.90 | 631 | 599 | 1,339 | 632 | 91 | 11 |
| | >0.90-1.20 | 401 | 273 | 171 | 74 | 21 | 6 |
| | >1.20 | 906 | 132 | 134 | 86 | 17 | 13 |
| | Total | 8,127 | 6,353 | 23,283 | 40,313 | 14,427 | 3,058 |

The outcome data (Table 12) published by Day et al. (2015) suggest that, regardless of baseline VA, the modal postoperative visual acuity is 6/6 or better, which indicates that cataract surgery results in good visual outcomes for the majority of cases. The data also suggest an obvious ‘ceiling effect’: people presenting with poorer visual acuity on average achieve a greater magnitude of improvement than people who have comparably better preoperative visual acuity, as they have greater potential for improvement.

As a result, we found that, for those cases who do not experience a bad outcome, baseline VA and postoperative change in VA are linearly related (Figure 4). We use this linear relationship to calculate the expected VA of simulated people who experience a good visual outcome. Eyes achieving a good visual outcome in the model are simulated to have their VA improve by $-0.7315x - 0.0637$, where x is preoperative VA in LogMAR.

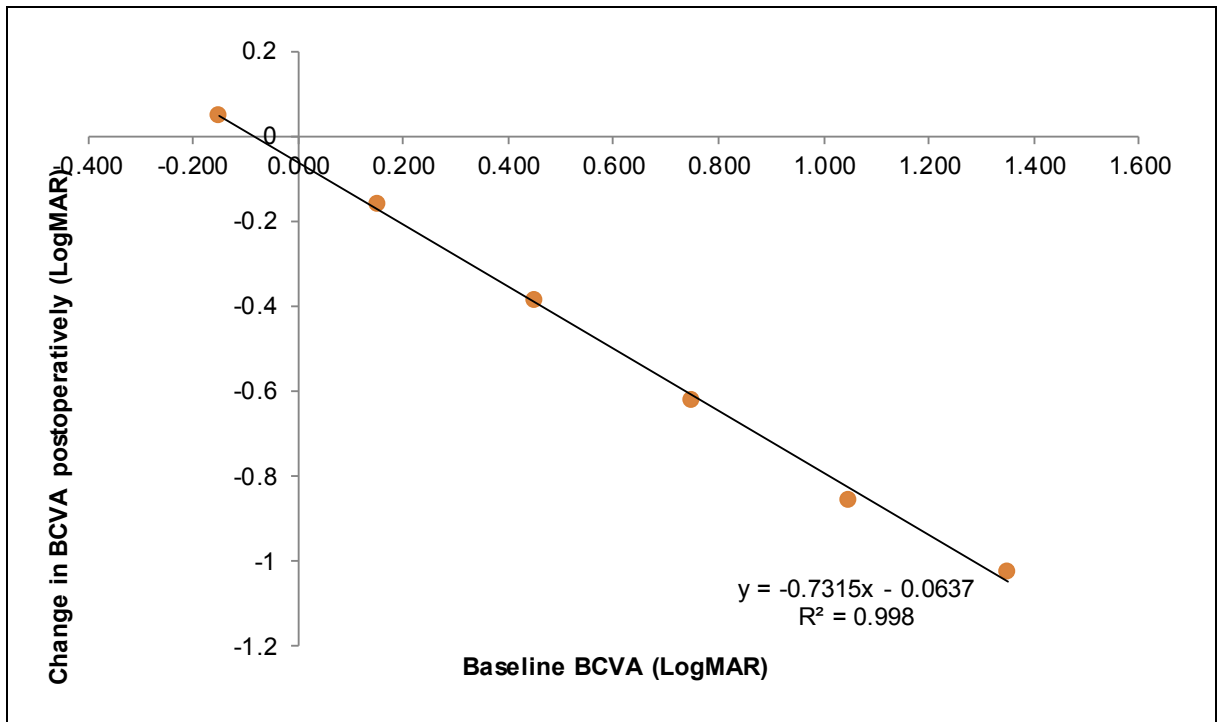


Figure 4: Linear regression of baseline BCVA and post-operative change in BVCA (logMAR units) in cases of good visual outcome

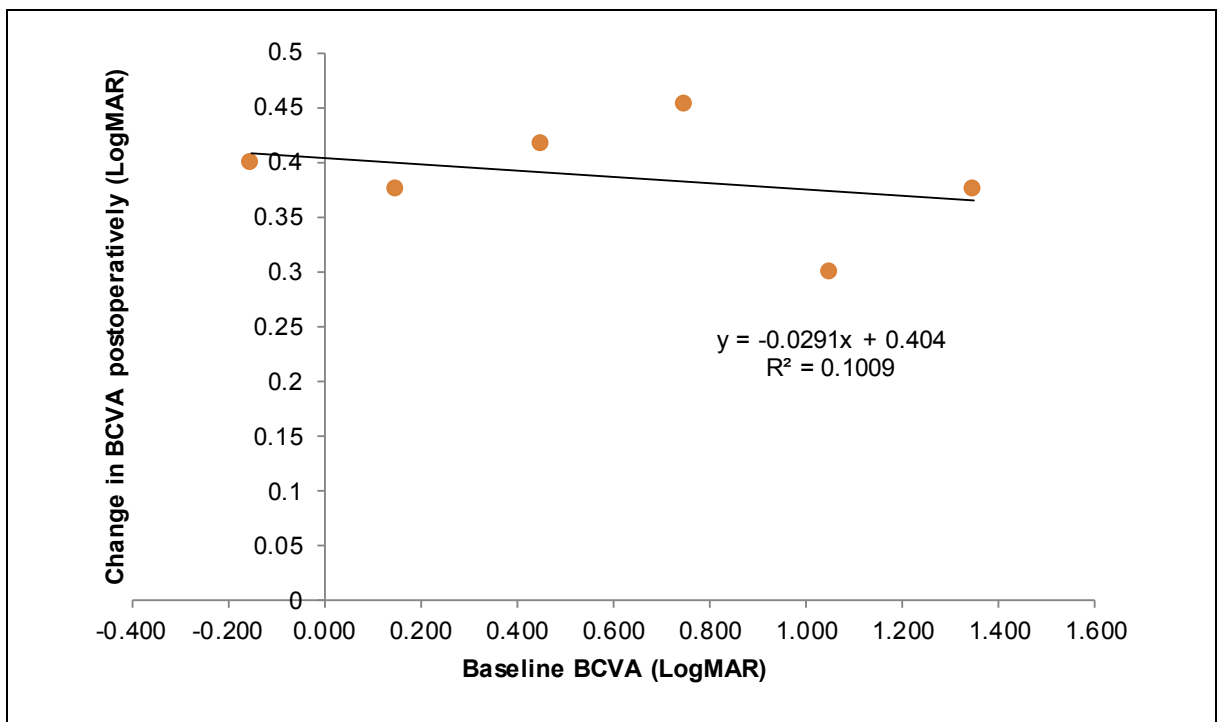


Figure 5: Linear regression of baseline BCVA and post-operative change in BVCA (logMAR units) in cases of poor visual outcome

For those cases where individuals experienced a poor outcome, there is no apparent relationship between baseline VA and postoperative change in VA (Figure 5). This possibly reflects the fact that those individuals with a poor visual outcome experience a magnitude of visual loss that is likely to be more dependent on the nature of their comorbidities and intraoperative complications (which have varying degrees of visual harm) than it is on their

baseline visual acuity. Because of this non-linearity, we derived the probability of transitioning to poor visual outcome as a weighted mean of the categorical transitions to poor outcome in Table 12. Therefore, eyes achieving a poor visual outcome in the model are simulated to have their VA deteriorate by 0.406 LogMAR units (this means an increase on the LogMAR scale).

J.3.3.3 Accounting for risk factors for good/poor outcome

Multivariate models using the RCOphth NOD dataset have been published which can be used to calculate the probability of good or poor visual outcome based on patient and eye-related factors. Sparrow et al. (2012) constructed 3 multivariate models to examine the risk factors associated with VA outcomes in people undergoing cataract surgery. The authors developed a logistic regression model to assess candidate indicators for poor (doubling of visual angle or worse) visual outcome. The model incorporated data from 12 NHS trusts, totalling 406 surgeons across 55,567 cataract operations undertaken between 2001 and 2006, for which post-operative VA outcomes were known for 40,758 (73.3%). All of the models adjusted for preoperative baseline VA as a continuous variable, and for inter-eye correlation by adjusting for paired eyes. The models incorporated the following covariates:

- age
- sex
- any ocular comorbidity
- age-related macular degeneration
- glaucoma
- diabetic retinopathy
- brunescient/white cataract
- high myopia
- corneal pathology
- amblyopia
- uveitis/synechiae
- no fundal view/vitreous opacities
- pseudoexfoliation/phacodonesis
- previous vitrectomy
- previous retinal detachment surgery
- axial length (quintiles)
- pupil size
- inability to co-operate
- unable to lie flat
- any alpha blocker
- tamsulosin, doxazosin, alfuzosin, indoramin, prazosin, terrazosin
- surgeon grade
- and PCR during surgery

Because of the large number of independent variables the models were limited to a main effects approach, and were generated using forward and backwards stepwise methods. The best-fitting visual loss model was one which included older age, short axial length, presence of ocular comorbidity, diabetic retinopathy, small pupil size and PCR during surgery as risk factors. We incorporated this model of clinically significant visual loss into our analysis.

Table 13: Multiple logistic regression model of risk factors for poor visual outcome (cf Sparrow et al. 2012)

| Variable | Adjusted OR (95% CI) |
|-----------------------------------|----------------------|
| Age | |
| <60 | 1.00 |
| 60–69 | 0.87 (0.54, 1.39) |
| 70–79 | 1.08 (0.72, 1.63) |
| 80–89 | 1.36 (0.91, 2.05) |
| 90+ | 1.93 (1.14, 3.29) |
| Axial length | |
| ≤22.37 | 1.51 (1.16, 1.96) |
| 22.38–22.95 | 0.99 (0.74, 1.31) |
| 22.96–23.47 | 1.00 |
| 23.48–24.18 | 0.97 (0.72, 1.29) |
| ≥24.19 | 0.77 (0.56, 1.05) |
| Any ocular comorbidity | |
| No | 1.00 |
| Yes | 2.28 (1.87, 2.77) |
| Diabetic retinopathy | |
| No | 1.00 |
| Yes | 1.73 (1.16, 2.59) |
| Pupil size | |
| Lg (>6.5mm) | 1.00 |
| Med (5.6–6.4mm) | 0.78 (0.57, 1.08) |
| Sm (<5.5mm) | 1.85 (1.26, 2.70) |
| Posterior capsular rupture | |
| No | 1.00 |
| Yes | 5.74 (3.93, 8.40) |

The National Cataract Dataset contains incidence data on even very rare occurrences of adverse events, but it is not possible to model each of these events in the absence of similarly granular information on predisposing factors. We therefore consulted with the guideline committee and, given the limitations of available evidence, it was agreed that the model should incorporate posterior capsular rupture (PCR), posterior capsule opacification (PCO), retinal detachment (RD), and endophthalmitis. We assume that other perioperative complications, such as CMO, corneal oedema, haemorrhage, iatrogenic glaucoma and others cannot be reliably predicted from preoperative characteristics, and are captured in the average cost of phacoemulsification reflecting their average rate of occurrence and cost impact.

J.3.3.4 Posterior capsular rupture

Posterior capsular rupture (PCR) describes the puncturing of the posterior lens capsule during cataract surgery and is an adverse event that increases the risk of downstream sequelae and poor visual outcome (Narendran et al., 2009; Sparrow et al., 2012; Day et al., 2015). As Table 7 shows, PCR is strongly associated with poor visual outcome. For this reason, and because PCR increases the probability that later adverse events will lead to additional costs and harms – even in otherwise uncomplicated surgeries with initially good visual outcomes – we also incorporated the model of PCR risk developed by Narendran et al. (2009) which used the same dataset as the model of poor visual outcome proposed by Sparrow et al. (2012).

Table 14: Multivariate logistic regression analysis of risk factors for PCR (cf Narendran et al. 2009)

| Variable | Adjusted OR (95% CI) |
|---------------------------------|----------------------|
| Age (ref: <60) | |
| 60-69 | 1.14 (0.84, 1.54) |
| 70-79 | 1.42 (1.08, 1.86) |
| 80-89 | 1.58 (1.20, 2.08) |
| 90+ | 2.37 (1.69, 3.34) |
| Male | 1.28 (1.13, 1.45) |
| Glaucoma | 1.30 (1.03, 1.64) |
| Diabetic retinopathy | 1.63 (1.24, 2.14) |
| Brunescent/white cataract | 2.99 (2.32, 3.85) |
| No Fundal view | 2.46 (1.70, 3.55) |
| PXF/phacodonesis | 2.92 (2.02, 4.22) |
| Pupil size (ref: large) | |
| Medium | 1.14 (0.95, 1.38) |
| Small | 1.45 (1.10, 1.91) |
| Axial ≥ 26.0 mm | 1.47 (1.12, 1.94) |
| Doxazosin | 1.51 (1.09, 2.07) |
| Unable to lie flat | 1.27 (1.11, 1.45) |
| Surgeon grade (ref: consultant) | |
| Associate specialist | 0.87 (0.67, 1.12) |
| Staff grade | 0.36 (0.17, 0.76) |
| Fellow | 1.65 (1.29, 2.11) |
| SPR | 1.60 (1.38, 1.85) |
| SHO | 3.73 (3.09, 4.51) |

J.3.3.5 Progression of VA decline in people with cataracts

Given the considerable history of cataract surgery and broad evidence base for its effectiveness, surprisingly few studies of long-term follow up of patients post-cataract surgery have been published. Similarly, age-related visual changes are typically referenced to a limited number of antiquated studies which have formed the benchmark for expected functional change in healthy eyes over time. In people who have cataracts which affect their vision, the natural history of cataract is poorly described.

Leinonen and Laatikainen (1999) investigated the rapidity of vision loss in eyes of 124 people on waiting lists for cataract surgery. The average waiting time from referral to surgery was 13 months. During a mean waiting time of 13 months, visual acuity in the study eye decreased from 0.68 logMAR to 0.96 logMAR. The average decrease in vision was 0.27 logMAR per year varying from none to 2.07 logMAR units. 30% of the eyes experienced worsening of vision by 60% or more. The percentage of persons with visual acuity of 0.5 or better in the better eye decreased from 66% to 41% and those with low vision (~ 0.3 in the better eye) increased from 8% to 21%. The mean waiting time in relation to the expected survival for all patients was 13% varying from less than 5% in 10 patients to more than 25% in 8 patients. The decline in acuity observed by Leinonen and Laatikainen (1999) is rapid, suggesting that for patients with moderate-to-severe VA impairment, a waiting time of 3 years for surgery could result in near-blindness in the affected eye. Even patients presenting with 6/6 vision

would be expected to decline to 6/96 in as little as 4 years. However, in this study, the mean waiting time for surgery was 13 months, and there is risk in extrapolating visual decline beyond that point. The committee related these data to their own clinical experience and agreed that the rates of decline in this small study were rapid, but that this was not unheard of in the real world. We also used this study to parameterise the rate of VA decline in eyes with asymptomatic cataract, which we based on the VA loss of 0.14 logMAR reported for 95 phakic fellow eyes.

Mönestam (2016) conducted a prospective, longitudinal, population-based cohort study detailing the visual acuity of patients at preoperative assessment, and at 5 yearly intervals thereafter to 15 years post-surgery (Figure 5). The study included 190 patients (83% of survivors). Fifteen years after surgery, the median CDVA in the operated eye had deteriorated from 20/20 postoperatively to 20/25. Sixty percent of the patients had worsening of CDVA of less than 0.1 logMAR units compared with postoperatively. These data provide an indication of the visual decline observed over long-follow up in pseudophakic eyes. Equivalent NHS data have not been published. We therefore use these data in our base case to model the trajectory of visual acuity change in the post-operative period until death as a constant linear decline. Leinonen and Laatikainen (1999) also publish data on the pseudophakic fellow eyes ($n=27$) of people on the waiting list, which declined by 0.07 logMAR over the 13 month of follow up. This is a more rapid decline than in Mönestam (2016) and, given the comparably short follow-up time of 13 months may reflect secondary cataract (PCO) rates.

We also used these data to complement the Leinonen and Laatikainen (1999) analysis in trying to establish a more conservative estimate for the rate of visual loss in people with unoperated symptomatic cataract and asymptomatic cataract. We do this by taking the ratio of the mean VA change in pseudophakic eyes between these 2 studies and then scaling the more rapid change in visual acuity in unoperated eyes in the Leinonen & Laatikainen (1999) study by this ratio. This produces 2 alternative profiles of visual acuity in untreated cataracts over time, according to baseline acuity. The committee considered these 2 profiles in relation to members' own experiences in clinical practice, and felt that the true average rate of visual decline was likely to lie somewhere between the profiles described in Figure 6. We therefore treat these data as representing the possible extremes of VA decline.

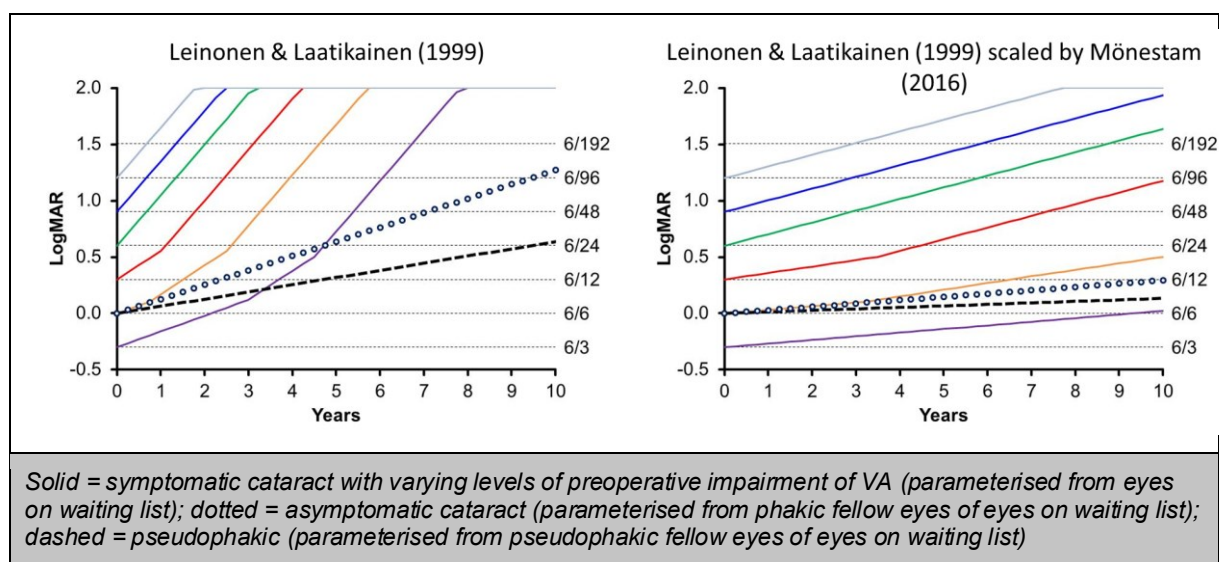


Figure 6: VA changes over time in eyes before and after cataract surgery

J.3.3.6 Simulating bilateral symptomatic cataract

In the model we assume the proportion of people who present with bilateral symptomatic cataract, which we define as the proportion of patients in whom vision-related quality of life

as defined by their bilateral cataract would indicate referral for bilateral surgery, is 60%. This is based on the RNIB campaign report from 2016, which reports that the maximum proportion of second eyes that were operated on within 1 year of first-eye surgery was 60%. We combine this with a study by Gollogly et al. (2013) who examined incident cataract surgeries in Olmsted County, Minnesota, between 2005 and 2011 and described the probability of second-eye cataract surgery using the Kaplan–Meier method. This suggests a short time-interval between first- and second-eye surgery in most cases, with ~60% of patients having the fellow-eye operated on three months after the index eye. We recognise that in the US healthcare system waiting times will be shorter and capacity greater than in the UK, but the data does provide a reasonable proxy measure (which agrees with the RNIB estimates) for the proportion of people who have symptomatic contralateral cataract at the initial referral. We use the slope of the Kaplan–Meier curve to calculate that an additional 10% of cases become symptomatic in the contralateral eye per annum after the peak at 60% (see Figure 7). The probabilities of developing symptomatic cataract are detailed in Table 15.

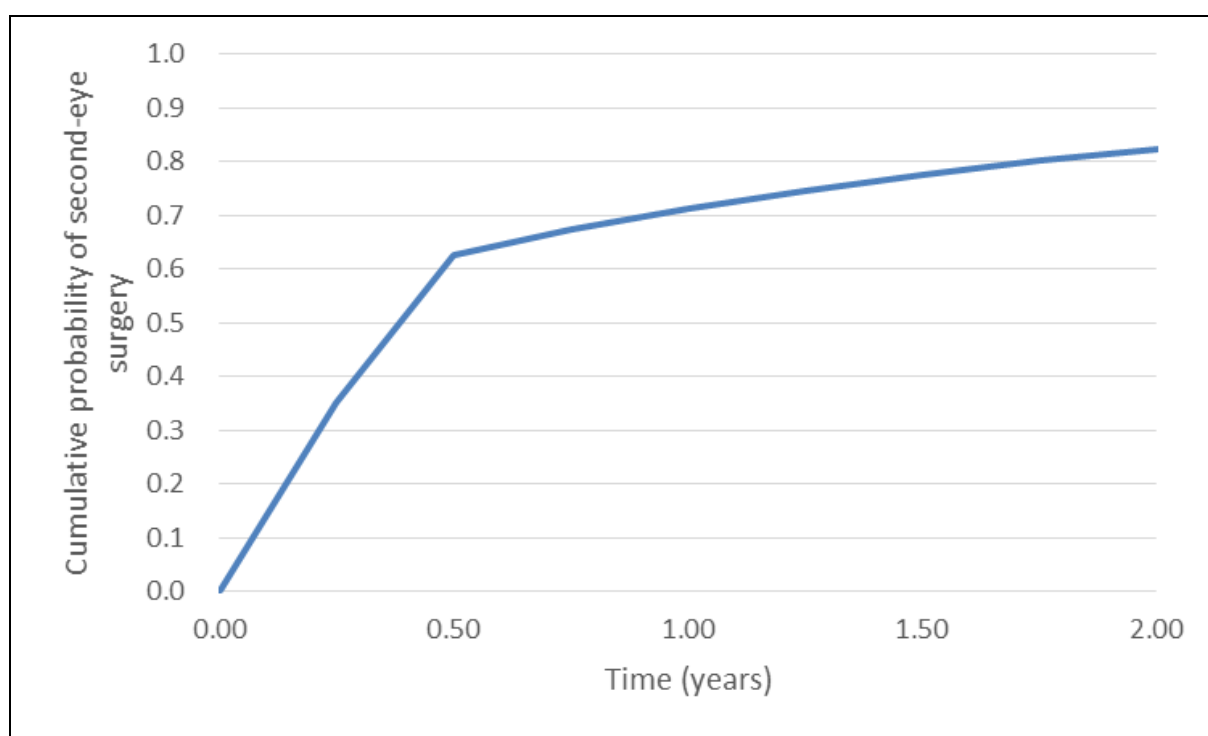


Figure 7: Cumulative probability of second-eye surgery

Table 15: Probabilities of developing symptomatic bilateral cataract

| Parameter | Estimate | Source |
|--|----------|---------------------------------|
| Proportion bilaterally symptomatic at presentation | 0.6000 | RNIB (2016) |
| Development of symptomatic cataract in second eye | | |
| Proportion symptomatic at 1 year | 0.7600 | Based on Gollogly et al. (2013) |
| Proportion symptomatic at 2 years | 0.8600 | |
| Probability of becoming symptomatic in 1 year | 0.417 | Calculated |
| Probability of becoming symptomatic in 1 cycle | 0.126 | Calculated |

J.3.3.7 Waiting list

We include a ‘waiting list’ state in the model, with a variable waiting time attached. This state is only active in the ‘immediate surgery’ and ‘delayed surgery’ strategies. In the immediate surgery arm, eyes with symptomatic cataract will enter the waiting list in the first cycle. In the

delayed surgery arm, eyes remain in the pre-threshold state until VA declines to a given threshold (e.g. 6/12) and transition to the waiting list state, or present with cataract meeting the threshold and immediately enter the waiting list.

The waiting list state incorporates a variable time in state which is set at 129 days in the base-case analysis as per the mean waiting time for surgery in the RNIB audit (2016). A paper by Desai et al. (1999) suggests that waiting times for first and second eyes were similar at ~7.5 months for either eye. These data are now 18 years old, and the current waiting time for NHS cataract surgery is different; however, it provides some indication that waiting times for first- and second-eye surgery do not systematically differ, so we use a single parameter for both in the model.

We assume that people with bilateral symptomatic cataract do not transition back to the waiting list state after their first eye surgery is performed, and therefore bilateral cataract surgery occurs within a three-month cycle in the model. The RCOphth NOD data presented by Day et al. (2015), gives an estimate of 3.7 months (range 0–114 months) between first- and second-eye surgeries for those patients who received second-eye surgery during the follow-up period - which is not the same as the average time between first- and second-eye surgery for all patients but does provide some justification for our assumption that bilateral surgery occurs within a single three-month model cycle. For those patients suitable for bilateral surgery, the waiting list state therefore functions as a constraint on the time taken to reach the bilateral surgery cycle, rather than having separate waiting times for each eye.

J.3.3.8 Retinal detachment

Phacoemulsification surgery increases the risk of retinal detachment by moving the vitreous gel located behind the posterior capsule, which in turn can place traction and shearing force on the retina and lead to tears or punctures that precipitate detachment (Haug, 2012). Day et al. (2016) undertook a subgroup analysis of the RCOphth NOD from 13 sites where data on both cataract and vitreoretinal surgery were recorded on the same electronic medical records system. The study included 61,907 cataract operations performed between October 2006 and August 2010. Analyses were restricted to cases with at least 3 months of potential postoperative follow-up. Pseudophakic RD surgery was performed on 131 eyes of 129 patients (0.21%; 95%CI 0.18%-0.25%). Of these, 36 were in eyes that had PCR during cataract surgery (3.27%; 95%CI, 2.37%-4.50%) and 95 were in eyes that did not have PCR (0.16%; 95%CI, 0.13%-0.19%). We used the lifetable published in Day et al. (2016) to produce Kaplan–Meier plots of time to Retinal Detachment following cataract surgery in eyes with and without PCR (Figure 8). The data support the assumption that the rate of retinal detachment over a 4 year period follows an approximately constant rate and can therefore be parameterised as a constant probability following surgery.

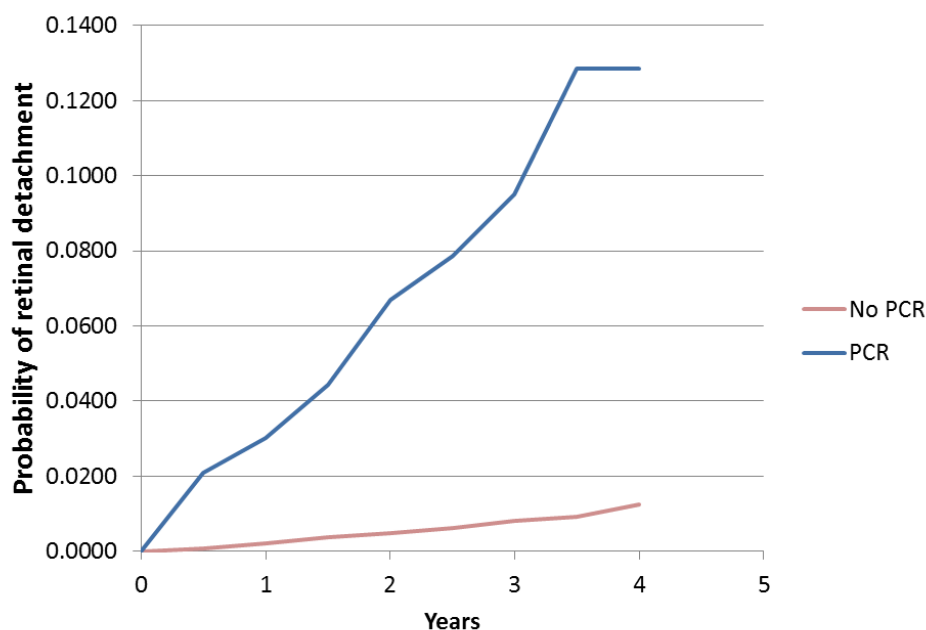


Figure 8: Kaplan-Meier plot of retinal detachment probability over 4 years, based on Day et al. (2016)

Table 16: Retinal detachment parameters

| Retinal detachment parameters | Value (95%CI) | Source |
|---|---------------|-----------------------|
| Events in first operated eyes | 0.0136 | Bjerrum et al. (2013) |
| Events in fellow eyes | 0.00032 | Bjerrum et al. (2013) |
| Rate ratio, pseudophakic -v- un-operated eyes | 4.22727 | Bjerrum et al. (2013) |
| Per-cycle probability of RD in general population | 0.0003 | Day et al. (2016) |
| 4-year probability of RD following phaco with PCR | 0.165 | Calculated |
| Per-cycle probability of RD following phaco without PCR | 0.0012 | Day et al. (2016) |
| Retinal detachment (general population) rate per 100 person years | 0.140 | Calculated |
| Retinal detachment (pseudophakic + PCR) rate per 100 person years | 4.498 | Calculated |
| Retinal detachment (No PCR) rate per 100 person years | 0.462 | Calculated |

Because retinal detachment can occur in phakic eyes a baseline risk of retinal detachment in the general population was taken from a large (n=202,226) Danish cohort study by Bjerrum et al. (2013) which corroborated the findings of a similar study from New Zealand (Russel et al., 2006). We calculated a relative risk of retinal detachment in operated compared with non-operated eyes from these data and applied this to the probability extracted from Day et al. (2016) to estimate the chance of retinal detachment in phakic eyes.

J.3.3.9 Endophthalmitis

Endophthalmitis is an inflammation of the internal layers or 'coats' of the eye which is typically infectious in origin. It can cause poor visual outcome, and usually requires biopsy, antibiotics, and in some cases an emergency vitrectomy. Although endophthalmitis is a

relatively rare side-effect of cataract surgery, it incurs additional costs and can have long-term consequences for HRQoL when visual acuity is affected. Based on analysis of the RCOphth NOD, Day et al. (2015) presented data from 19 centres on 145,868 cataract operations (81% of the total number of surgeries in the database) for which postoperative (within 3 months of cataract removal) incidence data on endophthalmitis were available. The rate of endophthalmitis within 3 months of cataract surgery was 0.03% (43/145,868 cases, 95% CI:0.02–0.04%). The rate of endophthalmitis was approximately 8 times higher (OR 7.94, 95% CI: 3.35–18.83) in cases with PCR than those without. This translates to 0.026% (2½ per 10,000 cases) without PCR and 0.21% (21 per 10,000 cases) with PCR. We used these rates to calculate the probability of endophthalmitis in cases of surgery with and without PCR in the model.

J.3.3.10 Posterior capsule opacification

Posterior capsule opacification (PCO) is a plaque which results from the growth and abnormal proliferation of lens epithelial cells which migrate to the posterior capsule. When the plaque approaches the central visual axis it causes visual-axis obscuration, resulting in dimness and clouding of vision. Symptomatic PCO is treated by a Nd:YAG laser capsulotomy, which involves using a laser to make a small hole in the posterior capsule that allows light through to the back of the eye, restoring normal vision. Whilst this is a common procedure, Nd:YAG capsulotomies also require additional outpatient visits which means they increase the overall cost of cataract surgery and therefore should be accounted for in an economic analysis. The clinical review for RQs 18 and 19 led the committee to recommend the use of hydrophobic IOLs to minimise the incidence of PCO and we therefore used this evidence to parameterise PCO rates in the model. The study by Sundelin et al. (2014) used Nd:YAG capsulotomy rates as a surrogate for PCO rates, using surveys and telephone interviews from 270 cases with a median follow-up time of 57 months (range 50–64 months). The 3-year cumulative incidence of PCO was 5.2% and the cumulative 5-year incidence was 11.9%, and a survival analysis of capsulotomy stratified by lens type suggests that it is reasonable to assume a constant rate of capsulotomies (and thus PCO) over time (Figure 7). We use this evidence to calculate the per-cycle probability of PCO.

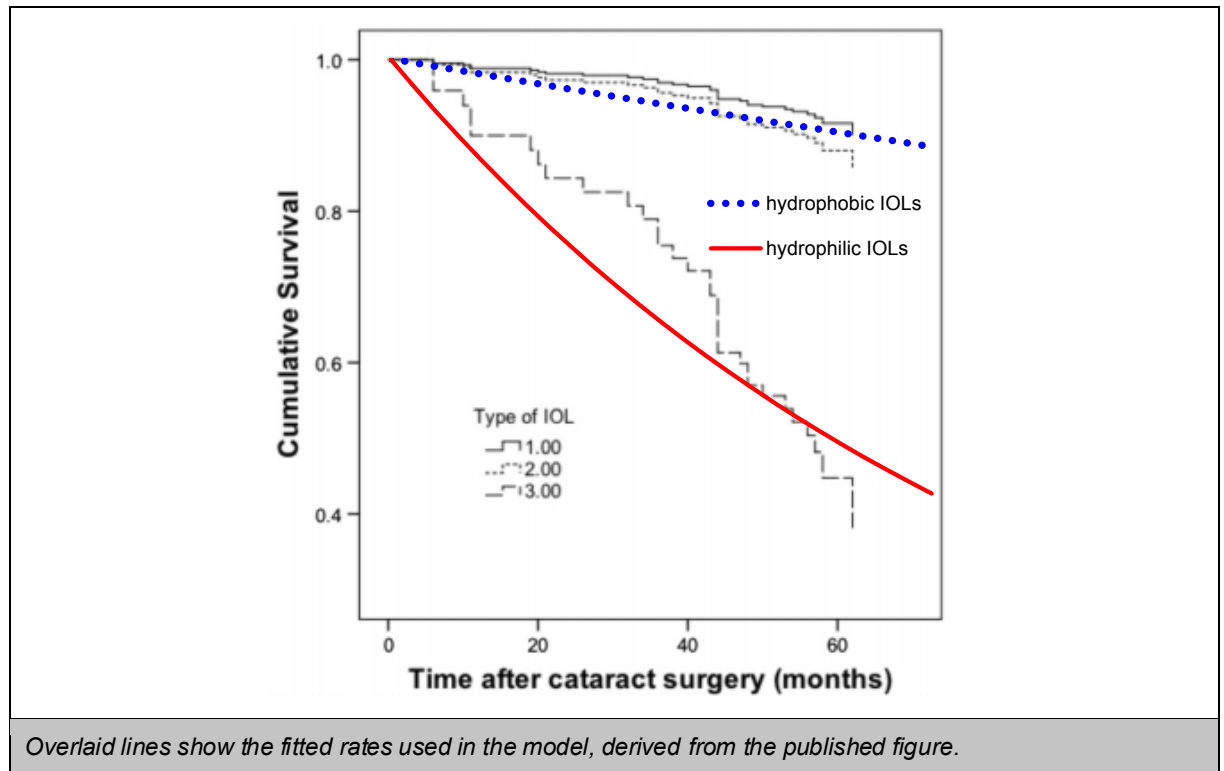


Figure 9 Kaplan–Meier plot of 5-year rate of Nd:YAG capsulotomy in Sweden (Sundelin et al. (2014))

J.3.3.11 Mortality

Mortality from all causes is estimated using national mortality statistics. Mortality is modelled using National Life Tables for England and Wales (2013–15). An increased mortality risk is included for patients with low vision, informed by a structural equation model developed using a dataset of recorded deaths in the US (Christ et al., 2008). The effect of having severe visual impairment – defined as being blind in both eyes – on mortality hazard, relative to no visual impairment, is characterised by a hazard ratio of 1.54 (1.28, 1.86). In the model, this hazard ratio is applied to patients whose VA is ≤ 1.20 logMAR letters in both eyes. The equivalent hazard ratio for people with some visual impairment (but not blindness in both eyes) is 1.23 (95% CI: 1.16, 1.31). In the model, this is applied to patients whose VA is less than 0.6 logMAR in either eye.

J.3.3.12 Resource use and costs

Our literature reviews sought to locate published economic evaluations or costing studies providing UK-specific resource use information of interest. Any remaining gaps in the resource use evidence were filled with estimates from the experts within the guideline committee, to which we can then apply appropriate unit costs.

The costs of each of the resource use elements within the model are obtained from a number of standard sources. Where these sources do not provide the unit cost needed, a search is conducted for unit costs generated from costing studies or within trials.

The Prescription Pricing Authority drug tariff database is used for prices of drugs. The database is updated monthly; therefore a single month's tariff is used for all parameters to maintain consistency.

NHS Reference costs are used as the source of unit costs for inpatient and outpatient procedures as well as hospital stay information.

The Personal Social Services Research Unit (PSSRU) generates the Unit Costs for Health and Social Care report which includes costs for both community and hospital-based healthcare staff.

Where an appropriate reference cost cannot be sourced from national tariffs and the cost variable used is from a relevant published study, the value is inflated to current prices using the HCIS inflation indices.

J.3.3.13 Costs of phacoemulsification cataract surgery with IOL implantation

The principal intervention in the model is phacoemulsification cataract surgery with intra-ocular lens implantation. This is the standard approach to cataract surgery. We spoke to experts on NHS Reference Costs and HRG grouping who confirmed it was reasonable to assume that the NHS reference costs would adequately describe the different lenses, medications, anaesthetics and intraoperative adverse events (aside from those requiring additional surgery and outpatient care) featuring in cataract surgery.

Table 17 Costs of phacoemulsification cataract surgery by HRG code and activity - NHS Reference Costs 2014-15

| Phacoemulsification cataract surgery: codes – BZ84A – CC Score 4+ BZ84B – CC Score 2-3 BZ84C – CC Score 0-1 | N (used for weighting) | Cost | Lower IQR | Upper IQR |
|--|---|-------------|----------------------------|----------------------------|
| BZ34A -- Elective Inpatients | 187 | £1,595 | £1,066 | £1,835 |
| BZ34B -- Elective Inpatients | 731 | £1,366 | £1,099 | £1,554 |
| BZ34C -- Elective Inpatients | 2,359 | £1,296 | £864 | £1,507 |
| BZ34B -- Contracted elective inpatient | 5 | £1,114 | £661 | £1,743 |
| BZ34C -- Contracted elective inpatient | 39 | £1,252 | £735 | £1,528 |
| BZ34A -- Day Case | 7,238 | £872 | £708 | £1,002 |
| BZ34B -- Day Case | 49,878 | £858 | £724 | £958 |
| BZ34C -- Day Case | 223,333 | £849 | £711 | £954 |
| BZ34A -- Contracted Day Case | 94 | £1,474 | £690 | £3,267 |
| BZ34B -- Contracted Day Case | 817 | £1,078 | £689 | £1,214 |
| BZ34C -- Contracted Day Case | 6,452 | £870 | £478 | £989 |
| Weighted average cost | | £858 | | |
| Cost with no PCR or endophthalmitis | | £849 | | |

J.3.3.14 Costs of posterior capsule opacification (PCO)

For PCO, we use the older NHS Reference Costs from 2013–14 as these contain a specific HRG code for capsulotomy which is not present in the most recent NHS Reference Costs schedule. With the agreement of the committee we used this older data and inflated the price to obtain a cost for 2014–15 using the PSSRU Hospital & community health services (HCHS) pay and prices index.

Table 18 Costs of Nd:YAG capsulotomy and management of PCO

| Lens capsulotomy codes- BZ04A – CC Score 1+ BZ04B – CC Score 0 | N (used for weighting) | Cost | Lower IQR | Upper IQR |
|---|---------------------------------------|----------------|----------------------|----------------------|
| Elective Inpatients -- BZ04A | 28 | £976.30 | £219.48 | £1,897.28 |
| Elective Inpatients -- BZ04B | 78 | £683.45 | £197.65 | £750.19 |
| Day Case -- BZ04A | 3,000 | £255.44 | £166.16 | £310.33 |
| Day Case -- BZ04B | 8,044 | £239.96 | £145.34 | £318.99 |
| Outpatient procedure -- BZ04A | 1,139 | £62.42 | £0.00 | £0.00 |
| Outpatient procedure -- BZ04B | 44,342 | £124.06 | £83.69 | £141.74 |
| Weighted average cost of Nd:YAG | | £147.76 | | |
| Inflated to 2014/15 | | £149.09 | | |
| Including 2 Outpatient Appointments | | £371.09 | | |

J.3.3.15 Costs of endophthalmitis

The committee agreed that 100% of endophthalmitis cases require a vitreous tap, which is performed in order to biopsy the causative organism and guide treatment. We derived a weighted average of the appropriate codes from the NHS Reference Costs 2014-15 as detailed in Table 14.

Table 19 Costs of endophthalmitis: vitreous tap

| BZ87A Minor Vitreous Retinal Procedures | N (used for weighting) | Cost | Lower IQR | Upper IQR |
|--|---------------------------------------|----------------|----------------------|----------------------|
| Elective inpatients | 28 | £2,383.39 | £661.43 | £4,246.85 |
| Day case | 1,152 | £637.19 | £404.74 | £789.03 |
| Nonelective short-stay | 38 | £730.17 | £259.99 | £845.18 |
| Weighted average cost of vitreous tap | | £680.23 | | |

Additional costs for endophthalmitis were taken from Kamalarajah et al. (2004). In this study cases were identified prospectively by active surveillance through the British Ophthalmological Surveillance Unit reporting card system, for the 12-month period October 1999 to September 2000 inclusive. Questionnaire data were obtained from ophthalmologists throughout the UK at baseline and 6 months after diagnosis. Their data suggest that 18% of patients require vitrectomy, and 38% of vitrectomies are performed urgently. We calculated a weighted average cost of vitrectomy from NHS Reference Costs, and then applied the incidence rates of surgical revisions as per Kamalarajah et al. (2004)

Table 20 Costs of vitrectomy derived from NHS Reference Costs 2014-15

| Major Vitreous Retinal Procedures BZ84A – CC Score 2+ BZ84B – CC Score 0-1 | N (used for weighting) | Cost | Lower IQR | Upper IQR |
|---|---------------------------------------|-------------|----------------------|----------------------|
| Elective inpatients -- BZ84A | 93 | £1,712.83 | £1,106.04 | £1,893.89 |
| Elective inpatients -- BZ84B | 194 | £1,832.37 | £1,280.85 | £2,103.95 |
| Nonelective inpatients -- BZ84A | 58 | £3,674.64 | £2,184.37 | £3,593.08 |
| Nonelective inpatients -- BZ84B | 71 | £2,527.02 | £1,512.26 | £2,911.58 |
| Day Case -- BZ84A | 906 | £693.58 | £296.72 | £1,067.04 |
| Day Case -- BZ84B | 3,842 | £685.54 | £296.45 | £988.20 |
| Nonelective short-stay -- BZ84A | 43 | £1,101.52 | £544.28 | £1,176.09 |
| Nonelective short-stay -- BZ84B | 260 | £1,126.49 | £845.20 | £1,411.20 |

| Major Vitreous Retinal Procedures BZ84A – CC Score 2+ BZ84B – CC Score 0-1 | N (used for weighting) | Cost | Lower IQR | Upper IQR |
|--|------------------------------|---------|--------------|--------------|
| Weighted average cost | | £847.68 | | |

Table 21 Rates of revisions and average cost of endophthalmitis

| Variable | Value | Source |
|---|-----------|---------------------------|
| Proportion of endophthalmitis patients requiring vitrectomy | 0.1831 | Kamalarajah et al. (2004) |
| Proportion of endophthalmitis vitrectomies undertaken urgently | 0.3846 | |
| Proportion of endophthalmitis vitrectomies requiring 1 or more revision | 0.1795 | |
| Proportion of endophthalmitis vitrectomies requiring 2 revisions | 0.0513 | |
| Proportion of endophthalmitis patients needing vitreous tap | 1.0000 | |
| Additional outpatient appts for endophthalmitis | 5.5 (4-7) | Committee |
| Additional costs of antibiotics, adjunctive steroids, repeat injections | £45.00 | Committee |
| Average cost of endophthalmitis | £1,627.74 | Calculated |

J.3.3.16 Costs of Retinal Detachment

Based on discussions with the committee we parameterised the average cost of retinal detachment as being described by a case mix of vitrectomies, 75% performed as a non-elective procedure, and 25% as an elective day case. This gives an average cost of £1,832.18.

J.3.3.17 Costs of PCR

We estimate the costs of PCR by updating the costs given in Qaternah et al. (2012), in which patients who had surgery in the 2-year period from April 2005, with a maximum follow-up to April 2009 were identified. Patients previously under review for ocular comorbidity apart from cataract were excluded. Each case with PCR was matched with an uncomplicated cataract operation performed on the same list by the same grade of surgeon. For both groups, details were extracted on of all additional subsequent visits and interventions. Data on the cost of visits and procedures were provided by the Department of Health. A total of 100 patients with PCT were matched with 100 controls. The preoperative parameters of the two groups were similar. The cases required a median of 3 (mean 3.6, range 0-24) additional postoperative visits compared with 0 (mean 0.19, range 0-8) for controls, with a median duration of follow-up of 74 (mean 129.5, range 6-1316) days for cases compared to 21 (mean 26.1, range 0-308) days for controls ($p=0.000$). The average cost of extra visits was £ 475.0 (SD £ 697.8) for cases and £ 69.2 (SD £ 51.0) for controls ($p<0.001$). The updated costs are detailed in Table 17.

Table 22 Costs of PCR (updated from Qaternah et al. 2011)

| Cost of PCR | Cost | 95%CI lo | 95%CI hi |
|---|----------------|----------|----------|
| Additional cost of PCR cases | £475.00 | £348.19 | £621.20 |
| Additional cost of non-PCR controls | £69.20 | £59.56 | £79.55 |
| Additional cost of PCR | £405.80 | | |
| Additional cost of PCR inflated to 2014/15 | £442.81 | | |

J.3.3.18 Costs of low vision

Vision-related healthcare resources are included in the model, required when a patient's VA reaches a threshold level of impairment. Previous CUAs in various areas of visual impairment have almost exclusively used estimates of the uptake of different low-vision resources collated by Meads et al. (2003), originally from various sources. This defines the proportion of people who register as sight impaired (94.5%), the uptake of low-vision aids (33%) and low-vision rehabilitation (11%), and the use of services to treat vision-related depression (39%) and hip replacements due to falls (5%). It provides estimates of the use of PSS resources, namely the use of community care by home care workers (6%) and entry into residential care (30%). It also provides estimates of the use of some non-NHS/PSS resources due to severe sight impairment: housing benefit and council tax benefit (45%), social security (63%) and tax allowances (5%).

In our model, low-vision resources are required when VA in the BSE is ≥ 1.20 logMAR (6/96) according to the relevant level of uptake listed above, with the exception of low-vision aids. The guideline committee advised that, in practice, low vision aids are used by all patients with VA of approximately ≥ 0.6 LogMAR (6/24) in their BSE and therefore we updated the proportion accordingly. These costs and proportions are detailed in Table 18. The non-NHS/PSS costs are included in a scenario analysis but not the base case.

Table 23 Costs of low vision, updated from Meads et al. (2003)

| NHS/PSS costs | Cost | Uptake % |
|---|------------|------------|
| NHS/PSS costs of blindness | | |
| Blindness registration | £153.40 | 94.5% |
| Low vision aids | £214.69 | 100% (33%) |
| Low vision rehabilitation | £323.30 | 11% |
| Depression | £2,478.95 | 39% |
| Hip replacement | £5,777.80 | 5% |
| Community care (home care worker) | £8,361.70 | 6% |
| Residential care (the 70% that is NHS/PSS funded) | £22,859.20 | 30% |
| Non-NHS/PSS costs of blindness | | |
| Housing and council tax benefit | £2,714.40 | 45% |
| Social security | £3,029.84 | 63% |
| Tax allowance | £502.35 | 5% |

J.3.3.19 Background costs

Evidence from trials included in the systematic review for RQs 24 & 25 on the effectiveness and timing of bilateral cataract surgery suggested that people who have second-eye cataract surgery may incur more non-cataract attributable costs to the health service compared with people with cataract who do not have surgery. The appropriate approach to so-called unrelated future costs and effects is a subject of current debate (see Morton et al., 2016). However, NICE's [Guide to the methods of technology appraisal 2013](#), on which the reference case for guideline development is based, states that '[c]osts that are considered to be unrelated to the condition or technology of interest should be excluded.' For this reason, we do not include any such costs in our base case, but we explore the impact of including them – either in the first year following surgery only or as a repeating annual cost – in a scenario analysis.

The costs for this scenario analysis were derived as follows. In the economic evaluations by Sach et al. (2007 & 2010), post-intervention overall service use was higher in the operated (first- and second-eye surgery) groups in the year after randomisation, particularly in the first 3 months after surgery. Significant differences in A&E attendances, outpatient visits, nurse

visits and GP visits were found between the two groups. We derived per-cycle resource use for these items from Sach et al. (2007 & 2010) and applied 2014-15 unit costs.

Table 24 Additional post-surgical primary and secondary care costs, by first- and second-eye surgery (scenario analysis only)

| Background cost parameter | Unit per annum or cost | Source |
|---|------------------------|-------------------------------|
| GP Visit | £36.00 | PSSRU 2016 |
| Practice nurse visit (assume 15mins) | £10.75 | PSSRU 2016 |
| Non-cataract outpatient appointment | | |
| Consultant-led first | £275.40 | NHS reference costs 2014–2015 |
| Consultant-led follow-up | £198.76 | |
| Non-consultant led first | £190.38 | |
| Non-consultant led follow-up | £152.33 | |
| Weighted average cost of outpatient apt. | £227.18 | Calculated |
| Average cost of inpatient bed-day | £597.39 | NHS reference costs 2014–2015 |
| First Eye | | |
| A&E attendances - surgery | 0.39 | Sach et al. (2007) |
| A&E attendances - no surgery | 0.12 | |
| Outpatient visits - surgery | 5.99 | |
| Outpatient visits - no surgery | 2.79 | |
| Inpatient bed-days - surgery | 3.13 | |
| Inpatient bed-days - no surgery | 1.16 | |
| GP visits - surgery | 4.72 | |
| GP visits - no surgery | 5.04 | |
| Nurse visits - surgery | 5.22 | |
| Nurse visits - no surgery | 3.40 | |
| Per-cycle secondary care costs -- surgery | £53.32 | |
| Per-cycle secondary care costs -- no surgery | £43.87 | |
| Per-cycle primary care costs -- surgery | £401.75 | |
| Per-cycle primary care costs -- no surgery | £161.95 | |
| Second Eye | | |
| A&E attendances - surgery | 0.29 | Sach et al. (2010) |
| A&E attendances - no surgery | 0.09 | |
| Outpatient visits - surgery | 6.94 | |
| Outpatient visits - no surgery | 2.81 | |
| Inpatient bed-days - surgery | 1.98 | |
| Inpatient bed days – no surgery | 1.79 | |
| GP visits - surgery | 4.44 | |
| GP visits - no surgery | 4.00 | |
| Nurse visits - surgery | 4.97 | |
| Nurse visits - no surgery | 2.93 | |
| Per-cycle secondary care costs -- surgery | £53.32 | |
| Per-cycle secondary care costs -- no surgery | £43.87 | |
| Per-cycle primary care costs -- surgery | £401.75 | |
| Per-cycle primary care costs -- no surgery | £161.95 | |

J.3.3.20 Quality of life

We recognise that the HRQoL implications of cataract are poorly described by visual acuity alone. However, we assumed that the degree to which changes in VA in both eyes over time directly influence HRQoL can be captured. In order to do this, we apply a regression model developed by Lansingh et al. (2009). Their model predicts TTO utility values given VA data, and is based on a previous study which attempted to describe TTO utilities for different Snellen ranges of visual acuity that made up a matrix of VA states (Brown et al. 2000). Using these data, they proposed a model which describes a third-order polynomial fit to the TTO utilities reported by Brown et al. (2000) which is illustrated in Figure 10 and given as:

$$\text{TTO Utility} = -0.0479x^3 + 0.191x^2 - 0.4233x + 0.9128$$

where x is LogMAR acuity.

The model fit is shown in Figure 10.

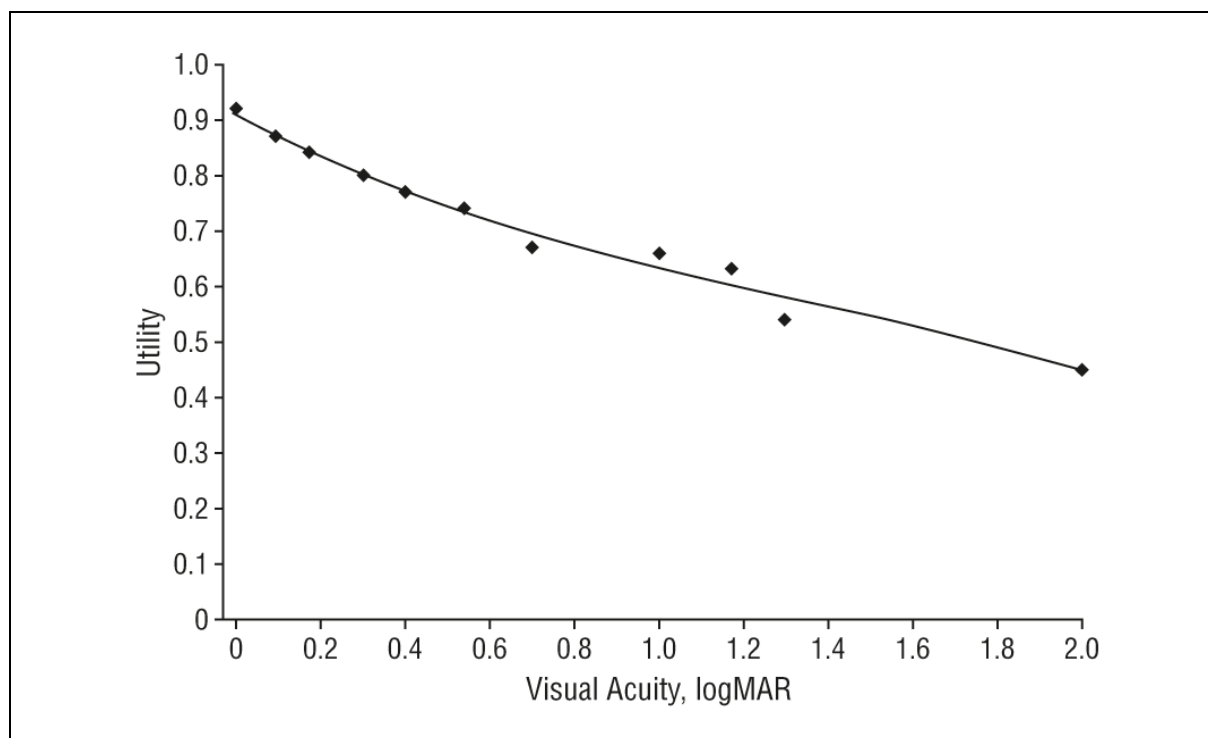


Figure 10: Third-order polynomial regression of VA on utility (from Lansingh et al., 2009)

We apply this model to both the better-seeing and worse-seeing eyes (BSE & WSE), and apply a weighting factor of 0.3 for changes in the WSE as per the recommendations of Scanlon et al. (2015).

In our model, QALYs are not gained through VA improvement after cataract surgery. The committee advised that many benefits such as ability to drive without glare, or improved colour perception, are not captured by visual acuity measures alone and therefore it was not appropriate to equate VA improvement with QALY gains. Instead the model considers the QALY losses that are prevented by cataract surgery, because the cataract removal avoids future loss of VA (in those people with a good visual outcome). Therefore, the model only accounts for the avoidance of that proportion of HRQoL that can be reasonably accounted for by VA loss.

J.3.3.21 Adverse events

We do not model adverse events as explicit states in the model but as events which occur at known incidence rates with cost and QALY losses applied to them on a per-cycle basis. Aside from changes in visual acuity-related quality of life, we were able to find evidence of QALY losses for retinal detachment and endophthalmitis. We acknowledge the limitation of not being able to simulate more adverse events, whilst also noting that other events are extremely rare.

J.3.3.22 Retinal Detachment

Rhegmatogenous retinal detachment is one of the most serious complications after phacoemulsification combined with intraocular lens implantation surgery, with vision-related quality of life (VRQoL), as well as visual acuity impacts that can be severe (Lina et al. 2016). However, little is known of the VRQoL in those retinal detachment patients after anatomical retinal re-attachment, especially whether or not the VRQoL is higher than that before cataract surgery. In a prospective case series study, Zhu et al. (2015) assessed the changes of VRQoL in age-related cataract patients who suffered from retinal detachment after phacoemulsification with intraocular lens implantation. All participants were asked to complete questionnaires in face-to-face interviews one day before and two weeks after cataract surgery, as well as one day before and three months after retinal detachment surgery. A total of 10,127 consecutive age-related cataract patients were followed up to 1 year after phaco-IOL implantation; among these patients, 17 were diagnosed with RRD. The average utility differential reported in Zhu et al. (2015) is 0.82 (95%CI = 0.69-0.95) which we applied as a multiplier to our modelled cohort in the cycle retinal detachment occurs but assumed no further retinal detachment related HRQoL losses are experienced beyond that point based on the committee's advice that RD is typically addressed within a 3-month period.

J.3.3.23 Endophthalmitis

Clarke et al. (2008) compared quality of life in Australian patients who developed endophthalmitis (19 cases) after cataract surgery between 1 January and 31 December 2003 with those who had uncomplicated surgery (31 controls). This study was retrospective (1 year post-surgery) and so therefore evaluates the chronic rather than acute HRQoL impact of endophthalmitis. The longer-term complications will be reflective of changes in visual outcome and therefore these values are of most interest given the structure of our model, although we acknowledge that this overlooks the acute effects of endophthalmitis, which may not be negligible. We assume that endophthalmitis incurs a QALY loss in the year in which it occurs, and that QALY decrement is then carried forward for the remaining life expectancy on the assumption that the chronic symptomatic consequences of endophthalmitis do not resolve.

Table 25: Endophthalmitis utilities (Clarke et al. (2008))

| | Mean utility score | -95%CI | +95%CI |
|-------------------|--------------------|--------|--------|
| Cases | 0.66 | 0.32 | 0.98 |
| Controls | 0.81 | 0.25 | 0.98 |
| Decrement = -0.15 | -0.15 | | |

J.3.3.24 Other HRQoL Issues

This model estimates the utility gain required in order for cataract surgery to be cost-effective across a range of different risk scenarios. These utility estimates are not tied to a single instrument, and quantifying the HRQoL of patients with visual problems is an evolving area of research. The committee expressed interest in the development of new surveys to measure HRQoL in people with cataract, and the validation of existing instruments in larger samples of people with cataracts than has previously been attempted.

The NICE Reference Case states the preferred measurement of effectiveness to be quality-adjusted life-years (QALYs), and the preferred tool for quantifying quality of life is the EQ-5D – a generic HRQoL survey which has a multidimensional scale. The EQ-5D is perhaps the most widely used generic HRQoL instrument and remains popular because it is short, captures information that can be combined with survival data and produces outputs which can be compared across health domains, which enables consistency in decision making using health economic models with threshold ICERs. Problems of vision, and in particular cataracts, have been singled out as exemplars of conditions which are not well quantified by generic tools in general and the EQ-5D in particular. A recent NIHR HTA monograph (Longworth et al., 2014) conducted a systematic review of studies using generic preference based tools in a range of ocular disease contexts, and found that, whilst some aspects of visual function (contrast sensitivity and visual acuity) were correlated with the VAS, TTO, HUI3 and SF-6D, the EQ-5D was not well correlated with either of these factors.

Disease-specific measures of QoL have the advantage of specificity – often they are designed to capture all the clinically important manifestations of a condition which impact QoL. However, it is not typically possible to compare measures of utility derived from disease specific instruments across conditions or populations, which in turn makes them difficult to incorporate directly into cost–utility models with a cost-per-QALY decision threshold. It has been argued that this is of lesser concern where the valuation of the descriptive system maintains a 0–1 (death–perfect health) scale and therefore should remain comparable across instruments (Longworth et al., 2014). However, even if that is the case, proponents of generic descriptive instruments have highlighted that condition-specific instruments are intrinsically reductive and therefore ignore important aspects of comorbidity which contribute to overall health in patients with conditions such as cataracts.

Disease-specific QoL instruments have additional value for research into cataracts because they provide data on symptoms that are not adequately quantified by clinical measurements of morbidity which, in problems of vision, are typically metrics of visual acuity and/or visual function. Patients with cataracts that have an impact on daily life (for example, by affecting driving ability, creating glare in certain conditions, or adversely affecting colour perception) may have deceptively good visual acuity scores. This is one reason why using simple visual acuity thresholds as a criterion for operating on a cataract has been criticised – it ignores the QoL implications of living with a condition which may never in fact manifest in a way that lowers visual acuity below an arbitrary threshold (Shandiz et al., 2011). It could be argued that patients who experience such symptoms would be expected to reflect them in their responses to generic form HRQoL instruments, but questions remain as to whether the granularity of response options is sufficient to capture the change in symptomatic terms either as a consequence of disease progression or positive change resulting from corrective surgery.

Four approaches to tackling these issues are possible. The first is to use a generic HRQoL instrument such as the EQ-5D and accept that there are problems of sensitivity to both the impact of cataracts on the responses to the dimensions of the tool and the likelihood that those scores will change in response to treatment. Another option is to compromise in order to maintain the desirable characteristics of generic instruments whilst attempting to make them more disease specific by adding extra dimensions which may measure a more specific manifestation of symptoms. A third option is to disregard the use of HRQoL surveys

altogether, and instead postulate that utilities generated from direct elicitation methods using, for example, TTO, can be mathematically related to visual acuity scores. Thus, a patient with a visual acuity of a given LogMAR value can be assigned a utility score from which a QALY value can be inferred. The ability to extract QALYs (which are comparable across health domains) is a benefit of generic HRQoL instruments as it means that data from them can be used in cost–utility analyses. Data from disease-specific instruments can seldom be used for such analyses, typically because the instrument scores lack the societal preference based valuation needed to transform them into QALYs. For this reason, several authors have proposed mathematical techniques which map the scores from a disease specific index to a generic tool such as the EQ-5D for the purposes of calculating QALYs. These mapping algorithms constitute a fourth possible approach to incorporating HRQoL data from patients with cataracts into economic models. This is a convenient methodology for extracting QALYs when they would otherwise not be available, but it does not address the fundamental problem that the index being mapped to may not be sensitive enough to capture changes in HRQoL from cataract surgery.

A 51-item Visual Function Questionnaire (VFQ) was developed in the United States using focus groups of patients with a range of ocular pathologies and subsequently reduced to a 25-item survey based on an analysis of the 51-item responses (Cusick et al., 2005). The NEI VFQ-25 has carer/physician administered and self-administered versions, and has been validated and used to show that those with ocular disease and accompanying visual impairment have lower scores compared with a reference group without ocular disease or visual impairment. The use of self-report questionnaires to substitute for visual acuity measurement has been limited, although the NEI-VFQ has been used in adult populations (aged 40 years or more) to show that those with visual impairment have lower scores compared with those without reduced visual acuity. However, concerns about the validity of certain sub-scales used in the NEI-VFQ and its range of measurement have been raised (Dougherty et al. 2010). In addition, use of the NEI VFQ in non-US populations is limited, especially amongst older populations who are likely to experience higher levels of visual difficulties than younger age groups.

Rentz et al. (2014) address some of the problems of mapping to the EQ-5D (predominantly the lack of sensitivity to visual acuity/visual function changes) by instead developing a shortened form of the VFQ-25 (which is not limited by insensitivity to changes in vision) that includes 6 domains: near vision, social vision; distance vision, role difficulty, vision dependency and mental health. The 6 domains were selected by applying Rasch analysis to the original VFQ-25 survey domains in order to eliminate problems of suboptimal psychometric validity – which includes, for example, the ability for patients to provide contradictory responses to multiple questions which are measuring similar properties. The resulting index, VFQ-UI, was then tested on multiple cohorts with 8 vignettes presented to a sample of the general population (n=607) in Australia, Canada, United Kingdom and the United States. The results suggest that the index is capable of producing health states that the general population consider as ranging across the continuum of perfect health to death. However, there are abnormalities in the predicted utility values which may be a function of the regression models used. The inclusion of age as a variable in the regression analysis is opaque – it is unclear whether this refers to the age of the valuers or the age of a patient described in the vignette. An additional anomaly is that the predicted utilities of patients increases with age as a consequence of the age coefficient, when it would typically be expected that healthy older patients would experience a baseline quality of life that is lower (as a consequence of ageing) than younger people (Kind et al. 1999). The index is relatively new, and thus far lacks validation and application in other studies. Further work is needed to establish its sensitivity to changes in HRQoL associated with cataracts, including their natural history and treatment.

We discussed these various approaches with the guideline committee, and produced example vignettes of how the VFQ-UI might reflect changes in HRQoL in patients with cataract. The committee stated that more work, in the form of trial and validation studies,

needed to be done in order for conclusions to be drawn on the best available method for measuring HRQoL in people with cataract. Establishing the impact of cataract and the benefit of cataract surgery in terms of QALYs gained remains an area of significant uncertainty.

J.3.3.25 Summary of included parameters

All parameters used in the model are summarised in Table 26, including details of the distributions and shape parameters. No probabilistic sensitivity analyses were undertaken for this work, so this table represents a library record.

Table 26: All parameters in original cost–utility model

| Parameter | Point estimate | Probabilistic analysis | |
|--|----------------------|------------------------|--------------------------------|
| | | Distribution | Parameters |
| Starting age | 77.1 (77.0, 77.2) | Normal | $\mu=77.10$; $\sigma=0.03$ |
| Sex (% male) | 0.407 (0.405, 0.410) | Beta | $\alpha=51838$; $\beta=75465$ |
| Postoperative LogMAR in pseudophakic eyes | 0.1 (0.1, 0.1) | Normal | $\mu=0.09$; $\sigma=0.02$ |
| 15-year LogMAR in pseudophakic eyes | 0.3 (0.2, 0.4) | Normal | $\mu=0.29$; $\sigma=0.05$ |
| Proportion bilaterally symptomatic at presentation | 0.600 (0.589, 0.611) | Beta | $\alpha=4807$; $\beta=3205$ |
| Proportion symptomatic at 1 year | 0.760 (0.751, 0.769) | Beta | $\alpha=6089$; $\beta=1923$ |
| Proportion symptomatic at 2 years | 0.860 (0.852, 0.867) | Beta | $\alpha=6890$; $\beta=1122$ |
| Proportion receiving surgery | n/a | n/a | n/a |
| Effects of surgery on BCVA | n/a | n/a | n/a |
| 1.20 < baseline LogMAR (worse than 6/96) | 0.3 (0.3, 0.3) | Normal | $\mu=0.32$; $\sigma=0.01$ |
| 0.90 < baseline LogMAR \leq 1.20 (6/48 to 6/96) | 0.2 (0.2, 0.2) | Normal | $\mu=0.19$; $\sigma=0.01$ |
| 0.60 < baseline LogMAR \leq 0.90 (6/24 to 6/48) | 0.1 (0.1, 0.1) | Normal | $\mu=0.12$; $\sigma=0.01$ |
| 0.30 < baseline LogMAR \leq 0.60 (6/12 to 6/24) | 0.1 (0.1, 0.1) | Normal | $\mu=0.06$; $\sigma=0.01$ |
| 0.00 < baseline LogMAR \leq 0.30 (6/6 to 6/12) | 0.0 (0.0, 0.0) | Normal | $\mu=-0.01$; $\sigma=0.00$ |

| Parameter | Point estimate | Probabilistic analysis | |
|--|----------------------|------------------------|--|
| | | Distribution | Parameters |
| baseline LogMAR \leq 0.00 (better than 6/6) | -0.1 | n/a | n/a |
| 1.20 < baseline LogMAR (worse than 6/96) | 1.7 | n/a | n/a |
| 0.90 < baseline LogMAR \leq 1.20 (6/48 to 6/96) | 1.4 | n/a | n/a |
| 0.60 < baseline LogMAR \leq 0.90 (6/24 to 6/48) | 1.2 (1.2, 1.2) | Normal | $\mu=1.20$; $\sigma=0.02$ |
| 0.30 < baseline LogMAR \leq 0.60 (6/12 to 6/24) | 0.9 (0.8, 0.9) | Normal | $\mu=0.87$; $\sigma=0.01$ |
| 0.00 < baseline LogMAR \leq 0.30 (6/6 to 6/12) | 0.5 (0.5, 0.5) | Normal | $\mu=0.52$; $\sigma=0.01$ |
| baseline LogMAR \leq 0.00 (better than 6/6) | 0.2 (0.2, 0.3) | Normal | $\mu=0.25$; $\sigma=0.003$ |
| Proportion of people losing vision | 0.012 (0.011, 0.014) | Beta | $\alpha=507$; $\beta=40251$ |
| Proportion of eyes having PCR | 0.019 (0.018, 0.020) | Beta | $\alpha=1067$; $\beta=54500$ |
| 4-year probability of RD | 0.023 (0.013, 0.042) | CLogNormal | $\mu=0.023$ $\sigma=0.304$ |
| Events in first operated eyes | 0.00136 | | |
| Events in fellow eyes | 0.00032 | | |
| Rate ratio, pseudophakic -v- unoperated | 4.23 (3.43, 5.20) | Lognormal | $\mu=1.442$; $\sigma=0.106$ |
| 4-year probability of RD following phaco with PCR | 0.165 | CLogNormal | $\mu=0.165$ $\sigma=0.346$ |
| 4-year probability of RD following phaco without PCR | 0.018 | CLogNormal | $\mu=0.018$ $\sigma=0.355$ |
| Hazard ratio for RD, PCR -v- no PCR | 35.8 (6.6, 194.4) | Lognormal | $\mu=3.578$ $\sigma=0.863$ |
| Prob of PCR in NOD | 0.020 (0.019, 0.020) | Beta | $\alpha=3514$; $\beta=176600$ |
| OR for Endophthalmitis given PCR | 7.9 (3.3, 18.8) | Lognormal | $\mu=2.07$; $\sigma=0.44$ |
| Prob of requiring Nd:YAG | 0.130 (0.092, 0.172) | Beta | $\alpha=35$; $\beta=235$ |
| Prob of requiring Nd:YAG given hydrophobic IOL | 9.4 (2.5, 35.5) | Lognormal | $\mu=2.24$; $\sigma=0.68$ |
| A&E attendances surgery | 0.3 (0.2, 0.4) | Lognormal | Lognormal: $\mu=-1.26$; $\sigma=0.19$ |
| Outpatient visits surgery | 6.9 (6.0, 8.0) | Lognormal | Lognormal: $\mu=1.93$; $\sigma=0.08$ |

| Parameter | Point estimate | Probabilistic analysis | |
|---|----------------------|------------------------|---------------------------------------|
| | | Distribution | Parameters |
| GP visits surgery | 4.4 (3.8, 5.1) | Lognormal | Lognormal: $\mu=1.49$; $\sigma=0.08$ |
| Nurse visits surgery | 5.0 (3.7, 6.5) | Lognormal | Lognormal: $\mu=1.59$; $\sigma=0.14$ |
| Proportion of endophthalmitis patients requiring vitrectomy | 0.183 (0.134, 0.238) | Beta | $\alpha=39$; $\beta=174$ |
| Proportion of endophthalmitis vitrectomies undertaken urgently | 0.385 (0.240, 0.540) | Beta | $\alpha=15$; $\beta=24$ |
| Proportion of endophthalmitis vitrectomies requiring 1 or more revision | 0.179 (0.077, 0.313) | Beta | $\alpha=7$; $\beta=32$ |
| Proportion of endophthalmitis vitrectomies requiring 2 revisions | 0.051 (0.006, 0.138) | Beta | $\alpha=2$; $\beta=37$ |
| Proportion of RDs requiring nonelective vitrectomy | 0.25 (0.06, 0.44) | Triangular | min=0.00; mode=0.3; max=0.50 |

J.3.4 Presentation and interpretation of results

The model includes 6 dimensions of data: baseline HRQoL, visual acuity in each eye, age, the probability of PCR, and the probability of visual loss. The possible combinations of these values runs into the several million, and therefore it is both sensible from the point of view of developing results that are useful to making recommendations, and desirable from a computational workload perspective, to rationalise these data by categorisation.

We developed cut-off points for these data by first designing a usable matrix arrangement of variables, drawing from visualisation principals used by Leal et al. (2009) in their development of life-expectancy tables for people with type 2 diabetes. For HRQoL, we use natural breaks to characterise low, moderate and good categories as 0.4/ 0.6/ 0.8. We illustrate profiles for these natural breaks using the VFQ-UI. The VFQ-UI has 6 dimensions. The first three dimensions are questions about how eyesight affects activities of daily living and ask the following:

- 1) How much difficulty do you have doing work or hobbies that require you to see well up close, such as cooking, sewing, fixing things around the house, or using hand tools? Would you say:
- 2) Because of your eyesight, how much difficulty do you have seeing how people react to things you say?
- 3) Because of your eyesight, how much difficulty do you have going out to see movies, plays, or sports events?

These dimensions are graded as:

1. No difficulty at all
2. A little difficulty
3. Moderate difficulty
4. Extreme difficulty
5. Stopped doing this because of your eyesight
6. Stopped doing this for other reasons or not interested in doing this

The fourth dimension of the VFQ-UI asks:

- 4) Are you limited in how long you can work or do other activities because of your vision?

This dimension is graded as:

1. All of the time
2. Most of the time
3. Some of the time
4. A little of the time
5. None of the time

The fifth and sixth dimensions of the VFQ-UI ask:

- 5) I stay home most of the time because of my eyesight.
- 6) I worry about doing things that will embarrass myself or others, because of my eyesight.

These dimensions are graded as:

1. Definitely True
2. Mostly True
3. Not Sure
4. Mostly False
5. Definitely False

For HRQoL, we use natural breaks to characterise low, moderate and good categories as 0.4/ 0.6/ 0.8. For illustrative purposes, a utility of 0.4 on the VFQ-UI would correspond to a health state of 323455 using the scoring methods described above, a utility of 0.4 would be described as health state 312445, and 0.8 as a health state of 211245. Exemplar VFQ-UI profiles are given in Subappendix Jc.

For visual acuity, we use the 6 categories of logMAR acuity (as Snellen equivalents) given in Table 12, for both the index eye (the eye to be operated on) and the fellow eye. Age is simplified into 3 categories with midpoints of 60, 75 and 90 years.

For the predicted probabilities of both PCR and visual loss, we used an iterative approach. Referring to the risk factor models previously described, we developed exemplar profiles with the lowest (no risk factors) and highest possible (all risk factors) predictive probabilities of PCR and visual loss, and then observed the changes in probability between these extremes as risk factors are added or removed from the model. Because these covariates are on logistic scales, the absolute risks of PCR and visual loss in low-risk and moderate-risk categories are much lower than some possible values of absolute risk for those profiles with many risk factors included. This is reflected in the midpoints adopted for low / moderate / high probability of PCR and visual loss which are set at 0.02 / 0.06 / 0.15 for both.

The cross-categorisation across 6 domains results in a matrix of 2,916 unique scenarios, each representing some combination of age, VA in the index eye, VA in the fellow eye, baseline HRQoL, risk of visual loss, and risk of PCR. It may be useful to imagine this matrix as generating a very large number of subgroup analyses, with the model calculating a categorical value of utility-gain for each of the cells in the matrix, which represent each possible combination of variables (the subgroups). The full matrices are published in Subappendix Jd, at the foot of this document.

These matrices show, for each possible combination of characteristics, the magnitude of immediate utility gain one would have to achieve in order to make surgery cost effective compared with no surgery or delayed surgery.

Each matrix has 2 axes. The x-axis running horizontal at the top of the matrix is divided into 3 parts from left to right, corresponding to the baseline HRQoL categories of low, moderate and good (0.4 / 0.6 / 0.8). In the stratum below this, there are 3 further subdivisions according to the risk of PCR (low, moderate, high). Each category of PCR risk is then subdivided into categories of risk of visual loss (low, medium, high). The y-axis running up the left vertical side of the matrix has a top-level stratum of 3 age categories (60, 75, 90).

These age categories are divided into 6 levels of visual acuity in the index eye (the eye to be operated) from 6/6 to 6/96, which are each subdivided into the same visual acuity categories for the fellow-eye. This means that each cell in the matrix represents the magnitude of HRQoL gain needed for surgery to be cost effective given a combination of categories of age, baseline HRQoL, VA in both eyes, risks of PCR and risk of visual loss.

We categorise the magnitude of HRQoL gain into the following brackets:

- None = surgery would be cost effective even if it conferred no immediate HRQoL gain
- Very small = greater than 0.00 but no more than 0.03
- Small = greater than 0.03 but no more than 0.06
- Moderate = greater than 0.06 but no more than 0.10
- Large = greater than 0.10

The rationale by which these categories were arrived at is detailed in Subappendix Jb.

These can be applied to any index. The recently developed VFQ-UI, which has a societal preference valuation like the EQ-5D meaning it can be used to generate QALYs in cost-utility analyses, is one option that addresses some of the challenges inherent in estimating the impact of visual impairment of HRQoL. Tables Jc.1–Jc.4 illustrate baseline and post-cataract surgery HRQoL scenarios corresponding to our categorisation of HRQoL scores (very small, small, moderate and large gains post-surgery) side-by-side using the VFQ-UI.

J.3.5 Sensitivity analyses

We undertook sensitivity analyses which changed some key parameters and costs in the model. Firstly, an analysis was run which included the background costs from Sach et al. (2010) as detailed in section J.3.3.19, with reference to first and second-eye surgery, the effect being to increase the overall cost of surgery. Secondly, the committee had discussed the different visual acuity thresholds proposed by some trusts as a means of rationing surgery. While a 6/12 threshold was common, in some trusts a 6/9 threshold had been proposed as an alternative so we undertook a sensitivity analysis to explore the impact of this lower threshold on the cost-effectiveness of immediate vs delayed surgery. Thirdly, we explored the importance of cataract progression, which in our model is simulated as the rate of logMAR decline in symptomatic eyes. In section J.3.3.5 we discuss the way in which VA decline is parameterised in the base-case analysis as a weighted function of two studies which represent extremes of rapid and slower decline. In the sensitivity analysis we use the unweighted (more rapid decline in VA) data from Leinonen and Laatikainen (1999) to explore the impact of a more rapid progression on the model results.

We discuss in section J.3.3.13 how we derived the cost of phacoemulsification cataract surgery. We spoke to experts on NHS Reference Costs and HRG grouping who confirmed it was reasonable to assume that the NHS reference costs would adequately describe the different lenses, medications, anaesthetics and intraoperative adverse events (aside from those requiring additional surgery and outpatient care) featuring in cataract surgery. Whilst we understand that the reference cost will incorporate, as a weighted proportion, the cost of more complex cataract surgery cases such as those requiring general anaesthesia, we have undertaken an additional sensitivity analysis that inflates the cost of phacoemulsification to account for these more complex cases. Our justification for doing this is twofold. Firstly, the precise mathematics of how the reference cost is calculated remains opaque, particularly with regard to how more complex cases are accounted for. Secondly, we have developed a model which explicitly deviates from considering the average level of benefit and instead considers the amount of benefit needed in many subgroups of risk factors for surgery to be cost-effective. It is appropriate therefore to explore the likelihood that higher-risk patients will incur higher than average costs, and examine the consequences of these additional costs on the model results. To this end, and in the absence of direct evidence of precise costs beyond

expert opinion, we include a sensitivity analysis which increases the costs of phacoemulsification by £500.

J.3.5.1 Probabilistic sensitivity analyses

Because of the model structure, and the departures therein from typical cost-effectiveness analyses as discussed in section A.2.3.1, we did not produce a full PSA. This is usually done to compare deterministic base-case results with probabilistically derived mean ICERs, and produce CEACs. However, in this case the model does not produce ICERs which can be used to inform recommendations for the RQs. It may be possible to run a PSA to develop confidence intervals around the utility values which populate the decision matrix, but those values are reported in categories rather than as point estimates and it is not clear how such an analysis would add value to how the model is used to answer the relevant review questions.

J.4 Original cost–utility model – base-case results

J.4.1.1 Results

We provide summary results for all 2,916 possible combinations of the categories described in J.3.4 in Subappendix Jd.

In summary, the majority of modelled profiles show that cataract surgery is cost effective even if there is no HRQoL gain, because immediate surgery avoids future QALY losses and costs incurred by leaving the cataract(s) to progress either until death (in the no surgery arm) or until a specified threshold value of acuity is reached. Where a gain in HRQoL is required it is in the majority of cases only a very small gain.

J.4.2 First-eye surgery

J.4.2.1 Immediate surgery compared with no surgery

The full matrix for immediate surgery compared with no surgery in the first eye is shown in Figure 26 in Subappendix Jd.

In an overwhelming majority of scenarios (>99%), cataract surgery is shown to be cost effective **even if it confers no immediate HRQoL gain**. This is because immediate surgery avoids future QALY losses and costs incurred by leaving the cataract(s) to progress until death.

There are only 6 exceptions to this rule, all of which involve people aged 90 who have no impairment of BCVA (6/6 vision) in the eye for which surgery is contemplated. If such people have **either** very good **or** very poor vision in their other eye, and they are at high risk of **both** PCR and visual loss, they would only be candidates for cost-effective surgery if it confers an improvement in their HRQoL that can be classified as at least 'very small' (that is, a utility gain of 0.00 to 0.03).

J.4.2.2 Immediate surgery compared with delayed surgery (threshold 6/12)

The analogous matrix for the comparison of surgery with delayed surgery in the first eye is shown in Figure 27 in Subappendix Jd. A relatively similar pattern is shown: most people (85% of scenarios) are predicted to benefit from immediate surgery even if it confers no HRQoL gain and, in those cases where a gain of HRQoL is necessary to justify the slightly higher cost of immediate surgery, this benefit only has to be of 'very small' (that is, a utility gain of 0.00 to 0.03) magnitude. There are a greater proportion of scenarios in which this kind of expectation is necessary:

- In 90-year-old patients, when BCVA in the index eye is unimpaired (6/6) and the risk of PCR and/or a poor visual outcome is high
- In younger patients, the scenarios in which a (very small) gain in HRQoL is needed are all those in which fellow-eye vision is 6/12. In these cases, it is most important to achieve an immediate gain in HRQoL when the risk of poor visual outcome is **lowest**; conversely, when the risk is high, no such gain is necessary. This is because, in this case, the risk only increases as the patient ages; therefore, delaying surgery until they meet a threshold is counterproductive. The same is not true in the oldest category because the lower life expectancy of 90-year-olds means that a nontrivial proportion of the cohort will die before they would qualify for surgery, and many of those that live long enough to reach the threshold will also have limited life expectancy after surgery. These factors combine to attenuate the risk in delaying surgery, and making overall cost effectiveness more strongly dependent on short-term outcome.

J.4.2.3 Examples

Example profile 1

In this example, we consider the case specified in Table 27, which is a typical example of the large majority of cases in which no immediate HRQoL is necessary to make surgery cost effective – a 75-year-old with a low risk of PCR and poor visual outcome, with moderate impairment of best-corrected visual acuity in the worse-seeing eye and some impairment of BCVA in the fellow eye. In this case, the referral would be for first-eye surgery in a case where both eyes have some degree of cataract. The VA threshold in the delayed surgery arm is set to 6/12 in this example.

Table 27: Example profile 1

| Variable | Value |
|------------------------------|--|
| Age | 75 |
| Starting BCVA (LogMAR), Eye1 | 0.60 (6/24) |
| Status of Eye1 | Symptomatic cataract (first-eye surgery) |
| Starting BCVA (LogMAR), Eye2 | 0.18 (6/9) |
| Risk of PCR | 0.02 (low) |
| Risk of poor visual outcome | 0.02 (low) |
| Starting HRQoL | 0.60 (moderate) |

Figure 11 details the modelled visual acuity trajectories of both eyes given immediate, delayed or no surgery. Because the first eye in this case is already past the 6/12 threshold or surgery the trajectories for the immediate and delayed surgical arms are identical for the first eye. In the no surgery arm visual acuity declines over time at the rate observed in Leinonen and Laatikainen (1999) scaled by the pseudophakic rate of VA decline in Mönestam (2016). For the second eye, the rate of decline in the no surgery arm and delayed surgery arm are identical, until the second eye has declined from 0.18 (6/9) to 0.3 (6/12) LogMAR, at which point surgery is simulated to take place, and the immediate and delayed surgery arms converge. The delayed strategy in this case incurs a loss of approximately 0.2 LogMAR before surgery, given the decline to 6/12 and then some further decline on the waiting list before surgery.

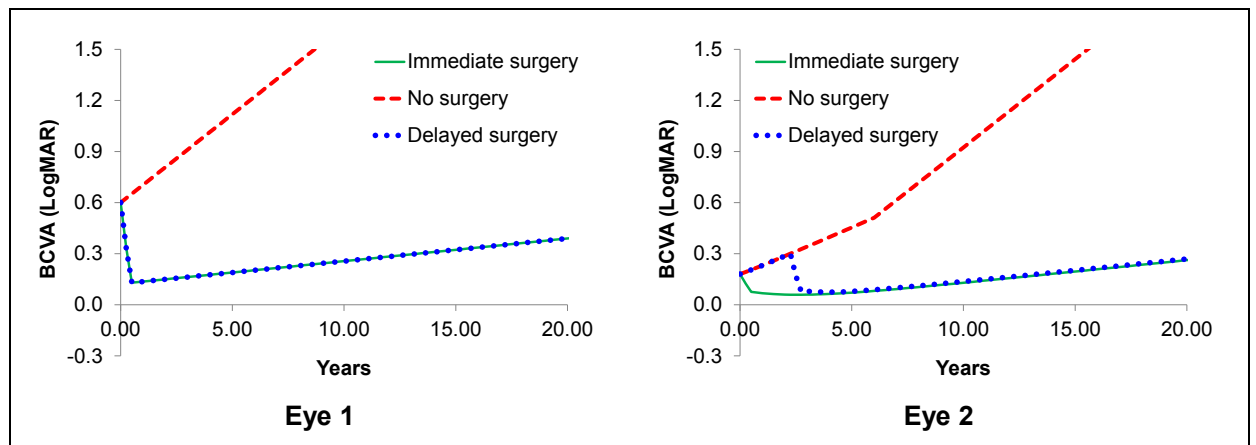
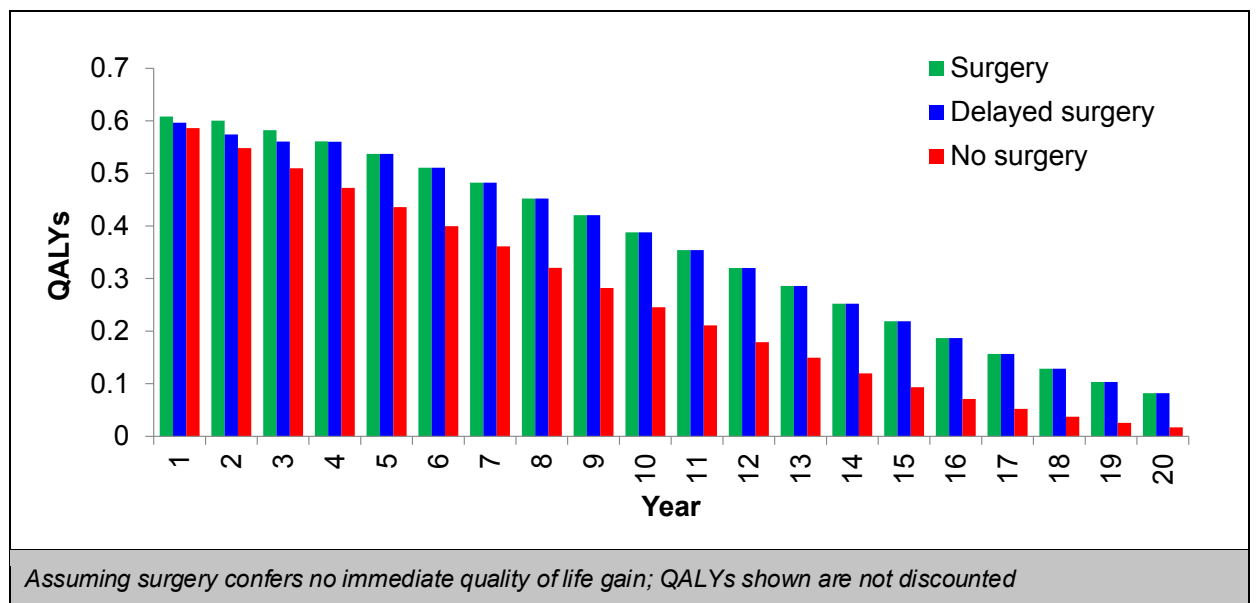


Figure 11: Visual acuity trajectories of both eyes for example profile 1 (base-case analysis)

Figure 12 compares these strategies in terms of QALYs (before any immediate HRQoL gain is applied to surgery). It can be seen that simply arresting the decline of acuity leads to discernible QALY gains for immediate surgery. Note the convergence in immediate and delayed surgery strategies after the VA threshold is met in the 3rd year. Beyond that point the rate of VA decline, and therefore HRQoL decline, is identical for these strategies.



Assuming surgery confers no immediate quality of life gain; QALYs shown are not discounted

Figure 12: Annual QALYs for each strategy in example profile 1 (base-case analysis)

Table 28 shows the base-case incremental cost-effectiveness results for example profile 1, and should be interpreted with the understanding that no immediate HRQoL benefit for surgery is included (in other words, no QALYs are gained in this analysis, but the degree to which they are lost over time is modified by the timing of surgery, making this the most conservative estimate possible of the cost effectiveness of surgery). The first thing to note is that 'no surgery' is the most expensive option simulated. This is because, in this instance, the costs of 'doing nothing' eventually substantially outweigh the costs of surgery, as the costs of low-vision support accumulate, resulting from unchecked decline in acuity. Because 'no surgery' is also associated with fewer QALYs than the surgical strategies, it is said to be dominated and can be dismissed as a feasible option.

The model estimates that performing immediate surgery costs an average of £112 more than delaying it until a threshold of 6/12 is reached (in this case, this is solely a result of

consequences for the second eye, as the first eye was already under the threshold at the time of presentation). This small saving comes from 2 places: the discounting effect of deferring costs for 3 or so years and the fact that a proportion of patients will die before they become eligible for second-eye surgery (whereas 96.6% of fellow eyes undergo eventual surgery in the 'immediate surgery' strategy, only 91.6% do if an acuity threshold is simulated). However, the extra money spent is predicted to confer a minimum of 0.057 QALYs compared to delayed surgery. For an outlay of just over £100, a return of over 0.05 QALYs would invariably be judged as extremely good value, with an ICER of £2,000 per QALY gained.

Table 28: Specimen base-case incremental cost-effectiveness results for example profile 1

| Strategy | Absolute | | Incremental | | |
|-------------------|-----------|-----------------|-------------|-----------------|---------------|
| | Costs (£) | Effects (QALYs) | Costs (£) | Effects (QALYs) | ICER (£/QALY) |
| Delayed surgery | £16,784 | 5.786 | | | |
| Immediate surgery | £16,896 | 5.843 | £112 | 0.057 | £1,946 |
| No surgery | £22,178 | 4.255 | £5,282 | -1.588 | dominated |

Assuming surgery confers no immediate quality of life gain

Example profile 2

In this example we consider the case of an 80-year-old with a high risk of PCR and poor visual outcome, but with relatively good visual acuity in both eyes (see Table 29). In this case, the referral would be for first-eye surgery in a case where both eyes have some degree of cataract. The VA threshold in the delayed surgery arm is once more set to 6/12.

Table 29: Example profile 2

| Variable | Value |
|------------------------------|--|
| Age | 80 |
| Starting BCVA (LogMAR), Eye1 | 0.2 (6/10) |
| Status of Eye1 | Symptomatic cataract (first-eye surgery) |
| Starting BCVA (LogMAR), Eye2 | 0.0 (6/6) |
| Risk of PCR | 0.15 (high) |
| Risk of poor visual outcome | 0.15 (high) |
| Starting HRQoL | 0.4 (poor) |

In this example (see Figure 13), the 'delayed surgery' and 'no surgery' arms track along the same trajectory until the threshold is reached for eye 1 and the transition to the waiting list and then surgery occurs. Because the VA in the second eye is better than eye 1, there is a longer period of decline along the no surgery trajectory in the delayed arm, reflecting the longer time taken for a cataract in a 6/6 eye to worsen to the VA threshold level.

Note that, in both eyes, the immediate and delayed surgery arms do not quite converge, which reflects the somewhat increased risk of visual loss of performing surgery when the patient is older than at baseline.

Patients with a lower VA at surgery stand to gain, on average, more VA than those patients who undergo surgery with good visual acuity (see J.3.3.2, and Day et al. 2015). Consequently, the model predicts that our example patient undergoing immediate surgery in eye 2 ends up with BCVA that is very slightly worse, in the immediate postoperative period,

than it would have been without surgery (this is just about discernible as the solid green line appears above the dashed red and dotted blue lines in year 1 in Figure 13).

Because of this, very slightly fewer QALYs are accrued in year 1 in the 'immediate surgery' arm than in the other arms. However, this initial small loss is offset as follow-up extends and the long-term benefit of early surgery accumulates (noting that, for the reasons discussed above, the QALY gain associated with delayed surgery is smaller).

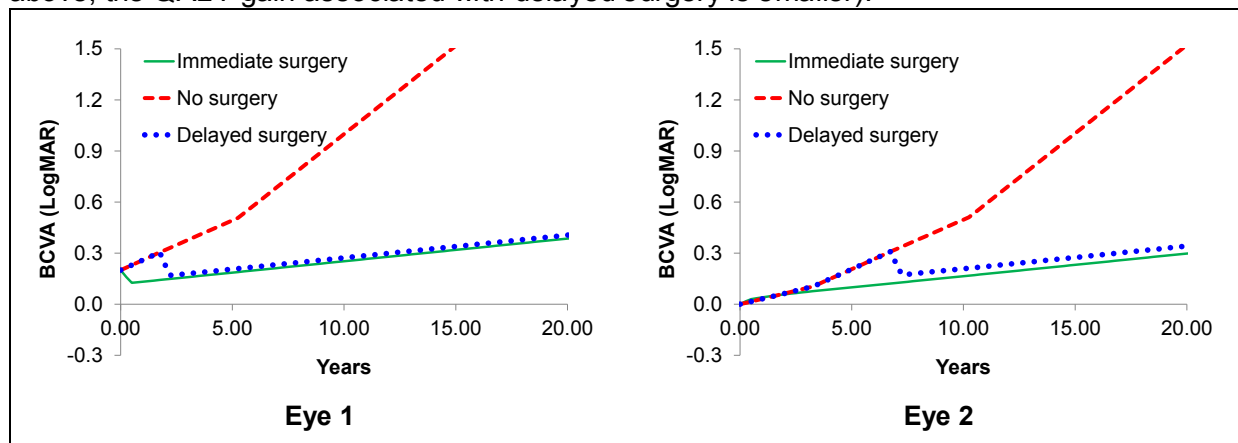


Figure 13: Visual acuity trajectories of both eyes for example profile 2 (base-case analysis)

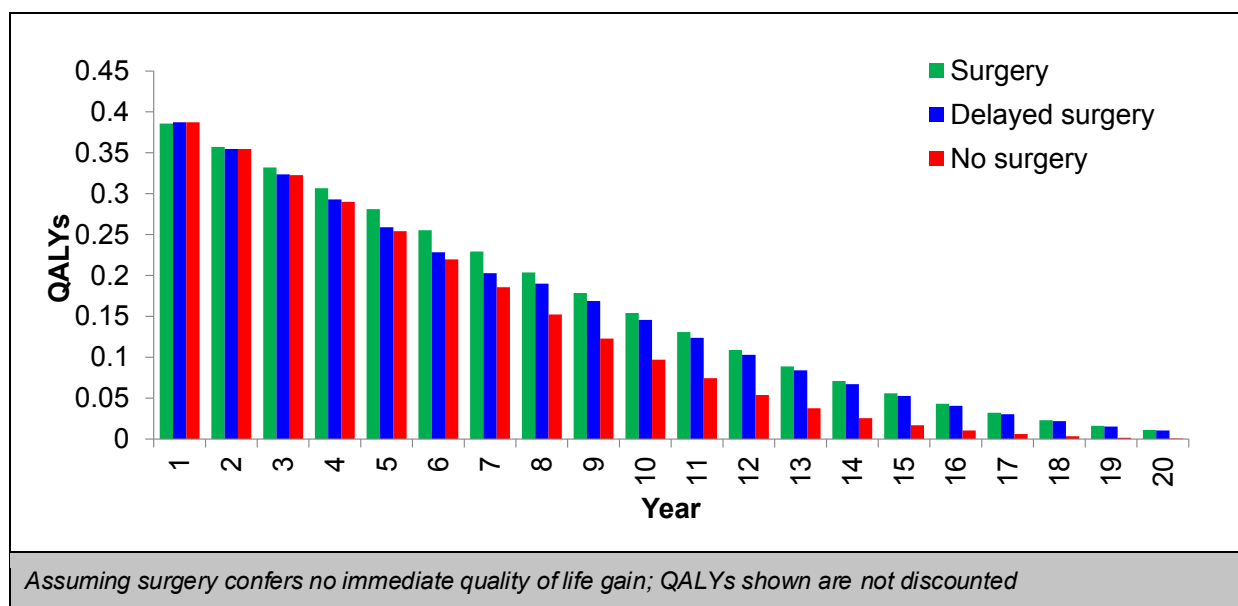


Figure 14: Annual QALYs for each strategy in example profile 2 (base-case analysis)

Table 30 provides the cost and QALY implications of each strategy for a population with this profile, which are then compared in a conventional incremental analysis. In contrast to profile 1, 'no surgery' is the cheapest option, because the better baseline acuity and shorter life expectancy of this profile means that people are likely to die before their sight declines to the level that would incur substantial support costs. Around a third of a QALY may be gained by offering deferred surgery (with a 6/12 BCVA eligibility threshold), at an additional cost of around £1,300, leading to a low ICER of less than £4,000 / QALY. However, greater incremental gains are available if immediate surgery is offered: for additional expenditure of a little under £700, compared with delayed surgery, over 1/8 QALYs are 'bought', at an ICER of around £5,000 / QALY. Again, this should be seen as excellent value for money, according to the NICE reference case.

Table 30: Specimen base-case incremental cost-effectiveness results for example profile 2

| Strategy | Absolute | | Incremental | | |
|-------------------|-----------|-----------------|-------------|-----------------|---------------|
| | Costs (£) | Effects (QALYs) | Costs (£) | Effects (QALYs) | ICER (£/QALY) |
| No surgery | £11,729 | 2.260 | | | |
| Delayed surgery | £13,026 | 2.597 | £1,297 | 0.337 | £3,847 |
| Immediate surgery | £13,704 | 2.726 | £678 | 0.128 | £5,278 |

Assuming surgery confers no immediate quality of life gain

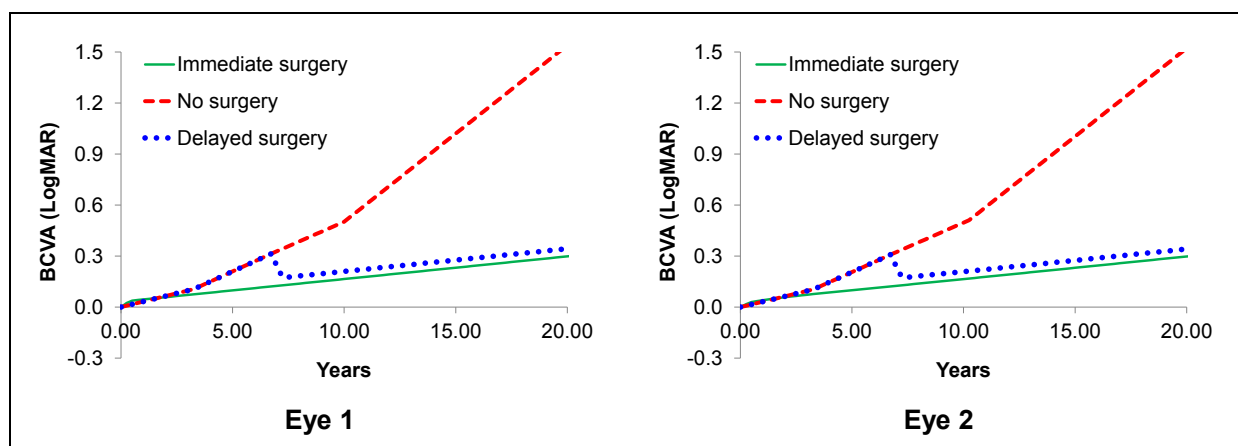
Example profile 3

Example profile 3 (Table 31) provides one of the very few examples in which some degree of immediate HRQoL benefit is necessary to render 'immediate surgery' cost effective compared with 'no surgery' or 'delayed surgery' (see J.4.2.1 and J.4.2.2). It represents an extremely unusual combination of characteristics in which a 90-year-old has a symptomatic cataract despite having no measurable impairment of BCVA in either eye, but the probability of PCR and visual loss is high.

Table 31: Example profile 3

| Variable | Value |
|------------------------------|--|
| Age | 90 |
| Starting BCVA (LogMAR), Eye1 | 0.0 (6/6) |
| Status of Eye1 | Symptomatic cataract (first-eye surgery) |
| Starting BCVA (LogMAR), Eye2 | 0.0 (6/6) |
| Risk of PCR | 0.15 (high) |
| Risk of poor visual outcome | 0.15 (high) |
| Starting HRQoL | 0.4 (poor) |

In this scenario, both eyes share some important features with eye 2 in example 2, above. The fact that immediate surgery means operating on 6/6 eyes means that it is associated with small short-term decrement to BCVA (and, by extension, QALYs). However, the fact that delayed surgery would not occur until some years into the future implies that the acuity result will never quite 'catch up' with what would have been achieved with earlier surgery. These features are shown in Figure 15.

**Figure 15: Visual acuity trajectories of both eyes for example profile 3 (base-case analysis)**

Again, we see 'immediate surgery' is associated with slightly attenuated QALYs in the initial follow-up period, but these are compensated for as time extends (Figure 16). The benefit of 'delayed surgery' – compared with 'no surgery' – becomes apparent in year 8, though does not reach the same level of QALY benefit as 'immediate surgery'.

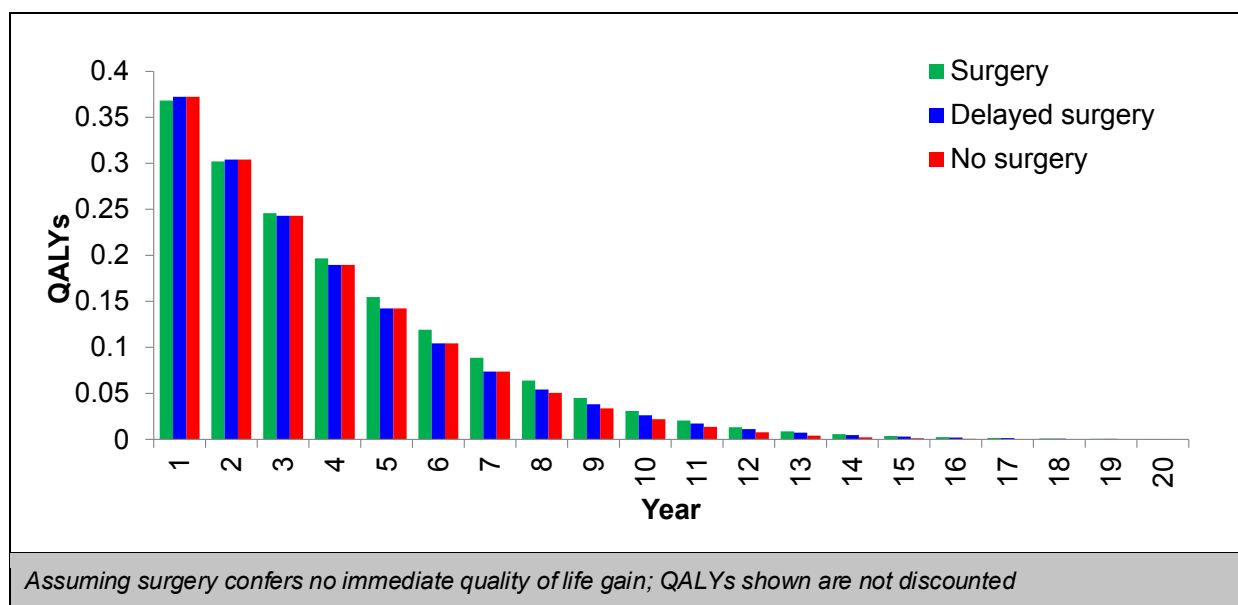


Figure 16: Annual QALYs for each strategy in example profile 3 (base-case analysis)

When the cost–utility results are subject to incremental analysis (Table 32), we see QALY totals in keeping with the above: 'delayed surgery' confers about 0.02 QALYs per person, compared with 'no surgery', and an additional 0.06 QALYs may be generated by offering surgery immediately. These gains come at costs of £300 and £1,500, respectively. This means that, assuming QALYs are valued at NICE's conventional value of £20,000 each, 'delayed surgery' would be considered cost effective compared with no surgery even if surgery confers no immediate HRQoL benefit. However, the additional QALYs provided by 'immediate surgery', compared with 'delayed surgery', come at a cost that exceeds this threshold, with an ICER of approximately £25,000 / QALY.

Table 32: Specimen base-case incremental cost-effectiveness results for example profile 3

| Strategy | Absolute | | Incremental | | |
|-------------------|-----------|-----------------|-------------|-----------------|---------------|
| | Costs (£) | Effects (QALYs) | Costs (£) | Effects (QALYs) | ICER (£/QALY) |
| No surgery | £6,170 | 1.420 | | | |
| Delayed surgery | £6,470 | 1.442 | £300 | 0.021 | £14,083 |
| Immediate surgery | £7,943 | 1.501 | £1,473 | 0.060 | £24,591 |

Assuming surgery confers no immediate quality of life gain

However, as noted above, results for this profile change if we assume that surgery results in a 'very small' HRQoL gain (increasing utility by 0.02; see Subappendix Jc for an example of the kind of change in visual function that might be expected to lead to this amount of benefit). Figure 17 and Table 33 show analogous model outputs to Figure 16 and Table 32, but with a HRQoL gain of 0.02 ascribed to surgery. It can be seen that the initial disbenefit of early surgery that is ascribable to BCVA loss alone is counterbalanced by the additional HRQoL gain, with the result that QALYs for 'immediate surgery' always exceed those for 'delayed surgery' or 'no surgery'. The lifetime discounted QALY total for 'immediate surgery' is more

than 0.1 QALYs greater than for the other options, with an incremental cost-per-QALY of around £13,000. 'Delayed surgery' also benefits from the assumed 'very small' HRQoL impact but, because the surgery event occurs in the future, when a large proportion of the population has died, and the gains are subject to discounting, it makes a smaller difference to results.

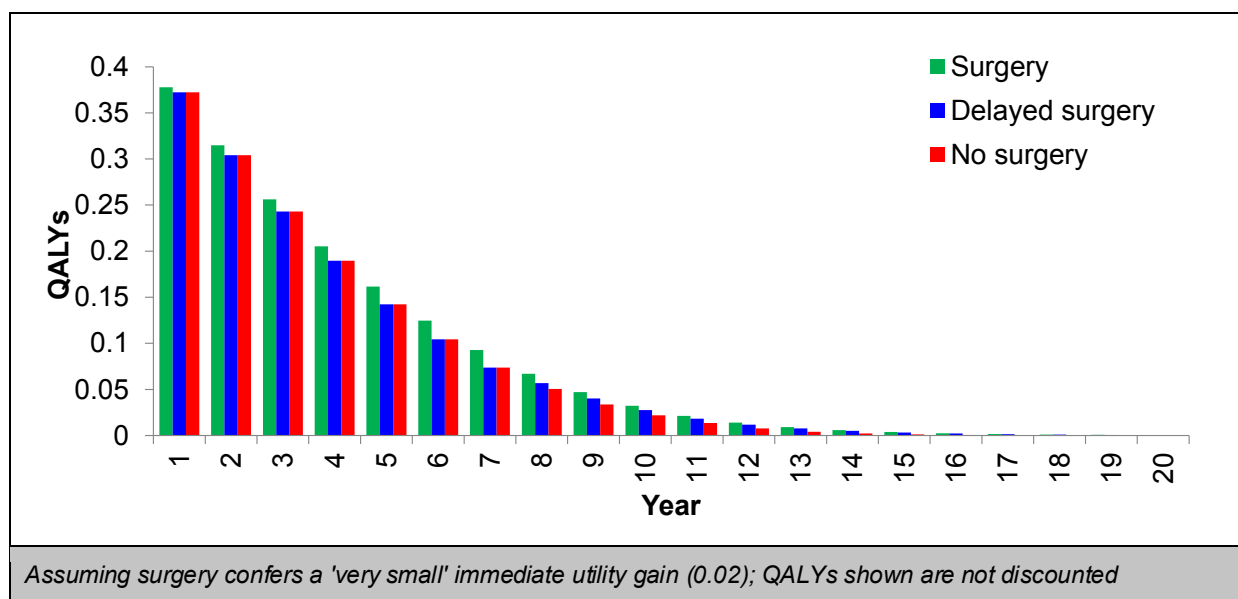


Figure 17: Annual QALYs for each strategy in example profile 3 (base-case analysis, with a 'very small' immediate quality of life benefit ascribed to surgery)

Table 33: Specimen base-case incremental cost-effectiveness results for example profile 3, with a 'very small' immediate quality of life benefit ascribed to surgery

| Strategy | Absolute | | Incremental | | |
|-------------------|-----------|-----------------|-------------|-----------------|---------------|
| | Costs (£) | Effects (QALYs) | Costs (£) | Effects (QALYs) | ICER (£/QALY) |
| No surgery | £6,170 | 1.420 | | | |
| Delayed surgery | £6,470 | 1.448 | £300 | 0.028 | £10,787 |
| Immediate surgery | £7,943 | 1.560 | £1,473 | 0.112 | £13,122 |

Assuming surgery confers a 'very small' immediate utility gain (0.02)

J.4.2.4 Sensitivity analyses

Faster rate of acuity decline

As explained in J.3.3.5, a rapid rate of acuity decline was observed in the Finnish waiting-list study on which we base the trajectory of unoperated eyes (Leinonen and Laatikainen, 1999); for this reason, in our base case, we scale these data by a factor that is derived from analysis of another Scandinavian study (Mönestam 2016). However, in this sensitivity analysis, we use the unscaled rate of decline.

Results (no full matrix shown) suggest uniformly that no immediate improvement in HRQoL is necessary to make surgery cost effective compared with no surgery or delayed surgery, irrespective of the individual's characteristics and ocular risk factors. This is predictable: if we believe unoperated eyes deteriorate at a rate of approximately 3 lines' BCVA per year (as

suggested in the Finnish data), there is an urgent impetus to offer immediate surgery rather than let people lose central vision in the eye in question.

Background NHS costs

When 'unrelated' costs are included (see J.3.3.19), cataract surgery becomes less cost effective. Full results matrices are provided in Subappendix Jd.

In the first version of this sensitivity analysis, these costs are assumed to apply in the first postoperative year only (this is the period for which there are empirical resource-use data; see J.3.3.19) and then revert to background level for subsequent years. Under this circumstance, 'immediate surgery' is still associated with an ICER under £20,000 / QALY compared with 'no surgery' in all scenarios featuring people under the age of 90, even when surgery is assumed to confer no immediate benefit to HRQoL (Figure 30). For some of the 90-year-old profiles, an immediate HRQoL benefit of 'very small' magnitude is necessary to make 'immediate surgery' cost effective and, in a very few cases where risk of both PCR and visual loss is high and BCVA in the index eye is unimpaired, the benefit has to reach a magnitude that could be classified as 'small' (see Subappendix Jc for illustrative examples of changes in visual function that might meet these definitions). For the comparison of 'immediate surgery' and 'delayed surgery' (VA threshold 6/12; Figure 31), a small number of scenarios in 60- and 75-year-olds require a 'very small' immediate benefit to favour 'immediate surgery'. Among 90-year-olds, most profiles require some degree of benefit and, in 3 cases (all where the index eye has excellent BCVA, the fellow eye has very poor BCVA and the risk of PCR and visual loss is high), 'immediate surgery' would not be cost effective compared with 'delayed surgery' unless a 'medium'-sized benefit can be expected.

In the second version of this sensitivity analysis, the additional, 'unrelated' costs are assumed to apply in all postoperative years. This has a clear effect on the estimated cost effectiveness of cataract surgery. As shown in Figure 32, 'immediate surgery' remains good value for money compared with 'no surgery' for all 60-year-olds and most 75-year-olds. However, when it comes to 90-year-olds, many cases would only be cost effective if an HRQoL benefit can be assumed and, in some cases, that benefit would have to be 'large' to outweigh the substantial additional lifetime costs that are now included. This requirement is even clearer when 'no surgery' is compared with 'delayed surgery' (Figure 33).

It should be emphasised that these sensitivity analyses represent a departure from the NICE reference case, which states that such costs should be excluded. If it is to be believed that receiving cataract surgery enables people to access healthcare resources for non-cataract conditions they would otherwise not have consumed, it should also be hoped that the additional healthcare is, in itself, cost effective and associated with benefits that cannot be estimated in this model. Nevertheless, the sensitivity analysis is useful as to illuminate model dynamics, which may remain opaque when almost all scenarios produce the same result.

Higher costs of cataract surgery

Raising the costs of cataract surgery has minimal effect on the model results for immediate first-eye surgery compared with no surgery. A few additional cases in 90 year olds where both the risk of visual loss and risk of PCR are high require a "very small" level of benefit in order to be cost-effective, particularly when the index and fellow eyes have visual acuity of 6/12 or better. When comparing immediate surgery with delayed surgery, the additional costs increase the number of cases in which a "very small" benefit is required in order for immediate surgery to be cost-effective. This is evident in cases where the fellow eye is at 6/9 and the risk of PCR is low, moderate or high but not when the risk of visual loss is also high. For people aged 90, the majority of cases require a benefit that is "very small" in order to offset the additional costs, except for those cases where visual acuity in the fellow eye is 6/6 and the risk of both PCR and visual loss is high, wherein a "small" benefit is necessary for immediate surgery to be the optimal strategy. For second eyes, the effect is similar to that

observed in first-eyes but in all cases of 90 year olds at any level of risk when acuity is 6/6 in both eyes a “very small” benefit is required. This pattern is also observed in the comparison between immediate and delayed surgery for second eyes.

Alternative – 6/9 – threshold for delayed surgery

A final sensitivity analysis explored the impact of a less stringent threshold for delayed surgery, LogMAR 0.18 (Snellen 6/9). A full results matrix for the first-eye decision-problem is shown in Figure 36 in Subappendix Jd. It shows that 'immediate surgery' is always estimated to be the optimal option in 60- and 75-year-olds. However, in the majority of scenarios among 90-year-olds, 'delayed surgery' represents a better balance of benefits and costs unless it can be assumed that surgery will make a difference to the patient's HRQoL that can be categorised as 'very small' or, when fellow-eye BCVA is severely impaired and risk of PCR and visual loss are both high, 'small' (see Subappendix Jc for illustrative examples of changes in visual function that might meet these definitions).

J.4.3 Second-eye surgery

J.4.3.1 Immediate surgery compared with no surgery

The full matrix for immediate surgery compared with no surgery in the second eye is shown in Figure 28 in Subappendix Jd.

As for the first eye, cataract surgery is shown to be cost effective in most scenarios **even if it confers no immediate HRQoL gain**. This is because immediate surgery avoids future QALY losses and costs incurred by leaving the cataract(s) to progress until death.

Compared with the first eye, there are slightly more scenarios in which HRQoL gain is necessary to produce an ICER lower than £20,000 / QALY; however, in common with the first eye, all these relate to people aged 90. In most cases, these scenarios also feature a high risk of visual loss. Whatever the other characteristics, an expectation of immediate HRQoL gain is needed when contemplating second-eye cataract surgery in a 90-year-old who has 6/6 vision in their fellow (pseudophakic) eye and a similar lack of impairment in their cataractous eye. Similarly, if risk of visual loss is high, immediate HRQoL gain is required for 90-year-olds whose index eye is severely impaired (6/96) and whose pseudophakic eye is moderately severely impaired (BCVA 6/24–6/48), though this does not hold for people with 6/96 impairment in both eyes (as they are subject to additional costs and mortality risk due to functional blindness, which can be relieved if surgery provides acuity gain in the index eye).

In all these cases, only a 'very small' immediate HRQoL benefit is required to make surgery cost effective.

J.4.3.2 Immediate surgery compared with delayed surgery (threshold 6/12)

The analogous matrix for the comparison of surgery with delayed surgery in the second eye is shown in Figure 29 in Subappendix Jd. A very similar pattern is shown: most people are predicted to benefit from immediate surgery even if it confers no HRQoL gain and, in those cases where a gain of HRQoL is necessary to justify the slightly higher cost of immediate surgery, this benefit only has to be of 'very small' magnitude. All these scenarios relate to 90-year-olds and most feature a high risk of visual loss.

J.4.3.3 Examples

Example profile 4

In this example, we consider the case of a 75-year-old with a moderate of PCR and poor visual outcome, with visual acuity for both eyes as described in Table 34. In this case, the

referral would be for second-eye surgery when first eye is pseudophakic (i.e has a history of cataract that has already been operated on, with an IOL implanted) and the second eye has an operable cataract. The VA threshold in the delayed surgery arm is set to 6/12 in this example.

Table 34: Example profile 4

| Variable | Value |
|------------------------------|-----------------------------------|
| Age | 75 |
| Starting BCVA (LogMAR), Eye1 | 0.00 (6/6) |
| Status of Eye1 | Pseudophakic (second-eye surgery) |
| Starting BCVA (LogMAR), Eye2 | 0.18 (6/9) |
| Risk of PCR | 0.06 (moderate) |
| Risk of poor visual outcome | 0.06 (moderate) |
| Starting HRQoL | 0.8 (good) |

In this profile (Figure 18), the pseudophakic first eye VA declines at a uniform rate while, as in previous examples, the VA in the 'delayed surgery' arm follows the 'no surgery' trajectory until 6/12 is reached and surgery occurs.

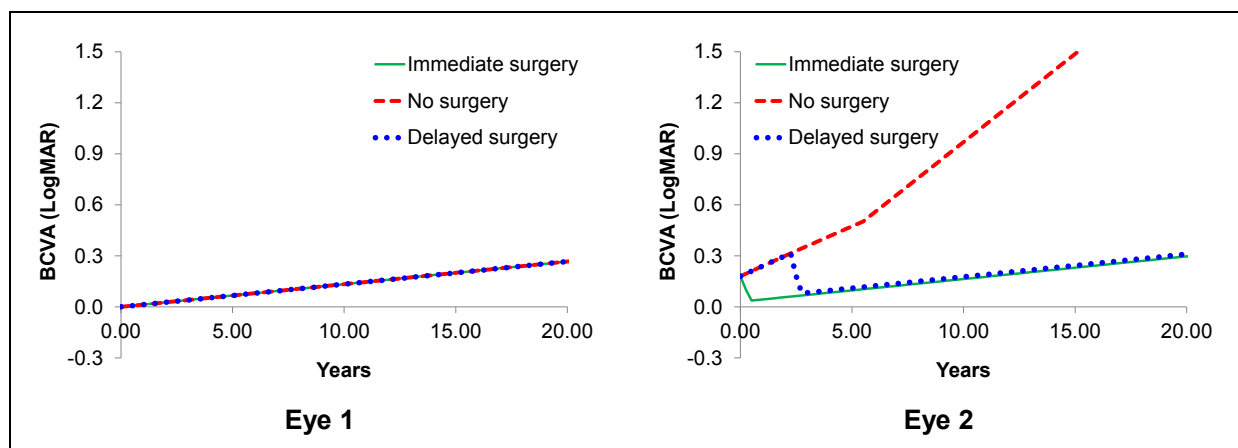
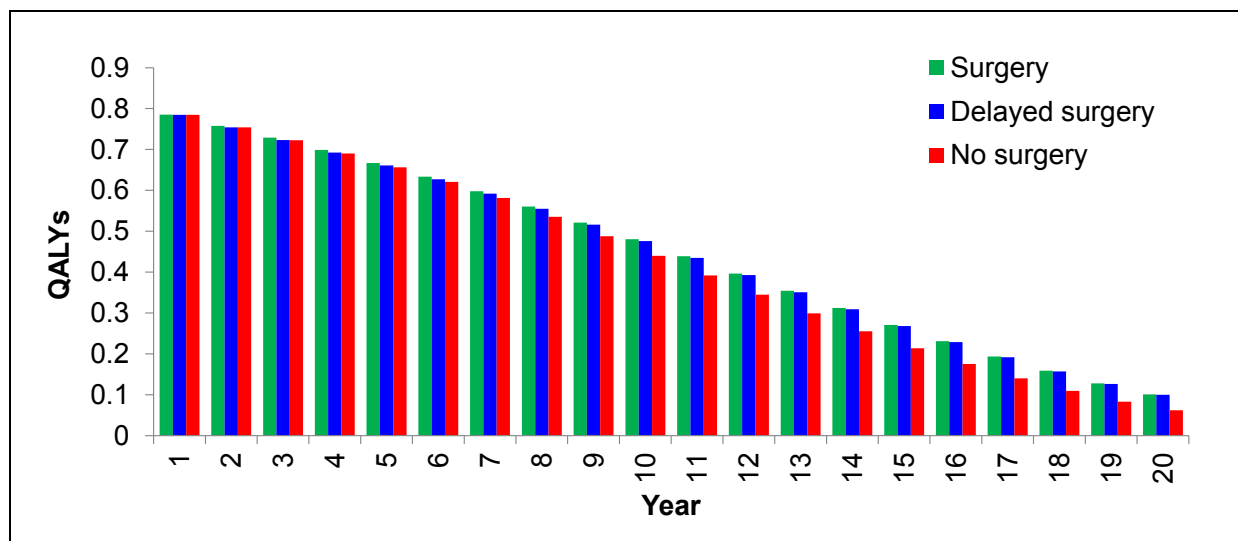


Figure 18: Visual acuity trajectories of both eyes for example profile 4 (base-case analysis)

Expected year-by-year QALYs for this scenario are shown in Figure 19.



Assuming surgery confers no immediate quality of life gain; QALYs shown are not discounted

Figure 19: Annual QALYs for each strategy in example profile 4 (base-case analysis)

Incremental cost–utility results for this profile are shown in Table 35. In this example, 'delayed surgery' is extendedly dominated. Extended dominance rules out any intervention that has an ICER that is greater than that of a more effective intervention. This is based on the assumption that decision-makers, when seeking to maximise value for money, will prefer the more effective intervention that has a lower incremental cost-effectiveness ratio thereby purchasing QALYs in a more efficient manner.

'Immediate surgery' is estimated to provide around 0.5 QALYs compared with 'no surgery', at an additional cost a little under £2,000, leading to an ICER of under £4,000 / QALY. If QALYs take NICE's usual valuation of £20,000 each, this would be seen as a strongly cost-effective intervention.

Table 35: Specimen base-case incremental cost-effectiveness results for example profile 4

| Strategy | Absolute | | Incremental | | |
|-------------------|-----------|-----------------|-------------|-----------------|---------------|
| | Costs (£) | Effects (QALYs) | Costs (£) | Effects (QALYs) | ICER (£/QALY) |
| No surgery | £17,491 | 6.799 | | | |
| Delayed surgery | £19,196 | 7.235 | £1,705 | 0.436 | ext. dom. |
| Immediate surgery | £19,349 | 7.295 | £1,859 | 0.496 | £3,749 |

Assuming surgery confers no immediate quality of life gain

Example profile 5

In this example, we consider a case that requires some immediate HRQoL benefit to justify second-eye surgery. The scenario – set out in Table 36 – is similar to example 4, except the population is now aged 90 and the risk of PCR and visual loss has become high.

Table 36: Example profile 5

| Variable | Value |
|------------------------------|-----------------------------------|
| Age | 90 |
| Starting BCVA (LogMAR), Eye1 | 0.00 (6/6) |
| Status of Eye1 | Pseudophakic (second-eye surgery) |
| Starting BCVA (LogMAR), Eye2 | 0.18 (6/9) |
| Risk of PCR | 0.15 (high) |
| Risk of poor visual outcome | 0.15 (high) |
| Starting HRQoL | 0.8 (good) |

In this profile (Figure 20), we again see uniform, gradual deterioration in the pseudophakic first eye

as in previous examples, the VA in the 'delayed surgery' arm follows the 'no surgery' trajectory until 6/12 is reached and surgery occurs.

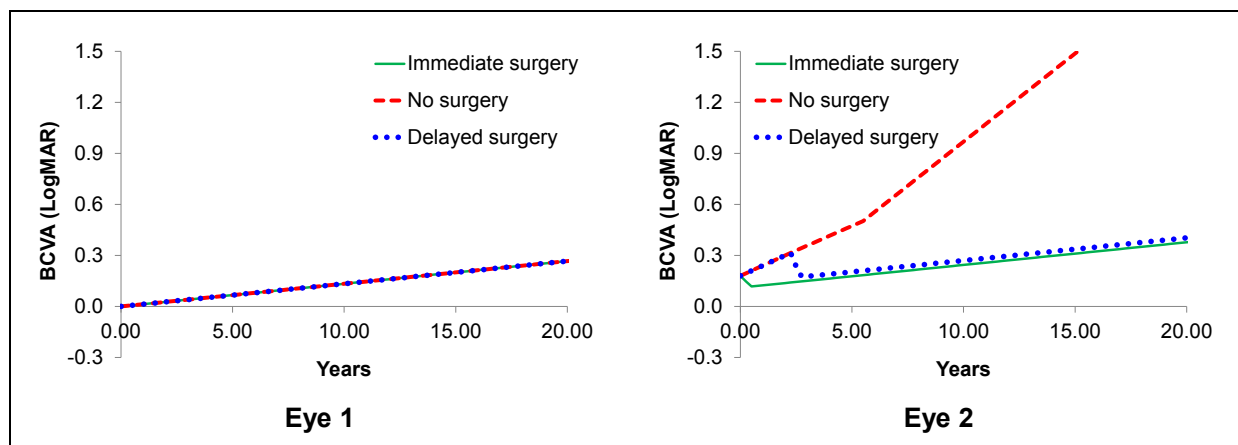


Figure 20: Visual acuity trajectories of both eyes for example profile 5 (base-case analysis)

Expected year-by-year QALYs are shown in Figure 21.

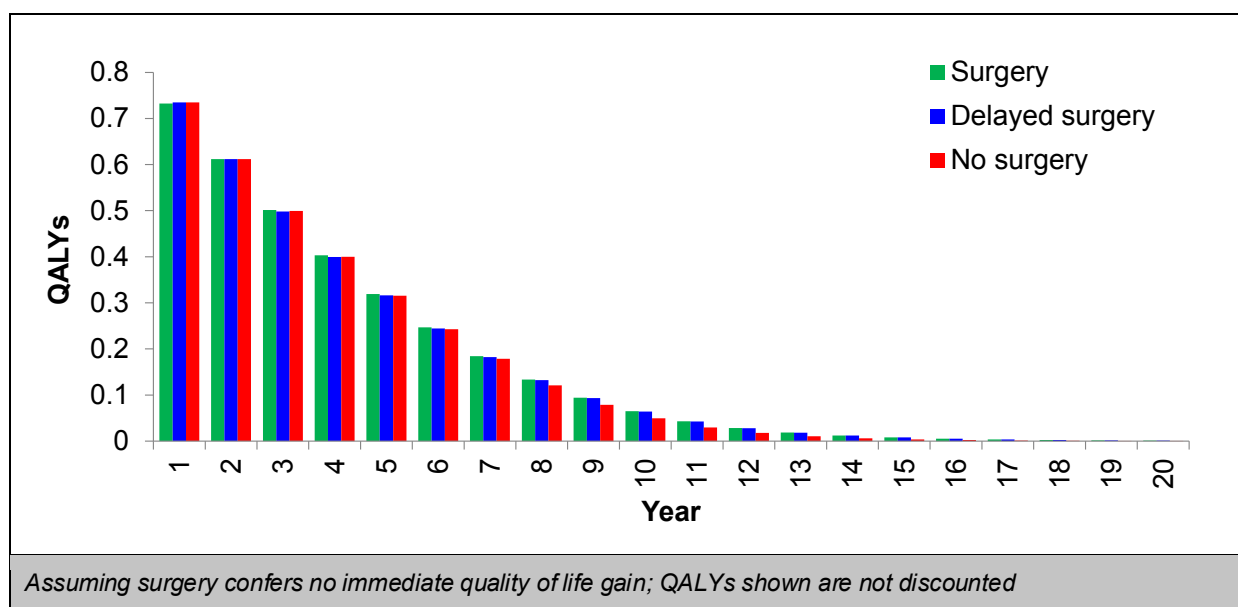


Figure 21: Annual QALYs for each strategy in example profile 5 (base-case analysis)

Incremental cost–utility results for this profile are shown in Table 37. In this case, the optimal strategy, assuming we do not want to pay more than £20,000 for additional QALYs, is 'delayed surgery'. In comparison, only a small benefit (around 0.01 QALYs) is gained by performing surgery immediately, and the associated cost leads to an ICER of very nearly £30,000 / QALY.

Table 37: Specimen base-case incremental cost-effectiveness results for example profile 5

| Strategy | Absolute | | Incremental | | |
|-------------------|-----------|-----------------|-------------|-----------------|---------------|
| | Costs (£) | Effects (QALYs) | Costs (£) | Effects (QALYs) | ICER (£/QALY) |
| No surgery | £7,386 | 2.981 | | | |
| Delayed surgery | £8,113 | 3.047 | £727 | 0.066 | £10,967 |
| Immediate surgery | £8,487 | 3.060 | £373 | 0.012 | £29,944 |

| Strategy | Absolute | | Incremental | | |
|---|-----------|-----------------|-------------|-----------------|---------------|
| | Costs (£) | Effects (QALYs) | Costs (£) | Effects (QALYs) | ICER (£/QALY) |
| <i>Assuming surgery confers no immediate quality of life gain</i> | | | | | |

However, as noted above, results for this profile change if we assume that surgery results in a 'very small' HRQoL gain (increasing utility by 0.02; see Subappendix Jc for an example of the kind of change in visual function that might be expected to lead to this amount of benefit). Table 38 shows incremental cost–utility results with a HRQoL gain of 0.02 ascribed to surgery. Here, the incremental benefit of 'immediate surgery' over 'delayed surgery' rises to around 0.04 QALYs, with no change in incremental costs, leading to an ICER a little under £10,000 / QALY. Therefore, if we are content to assume that surgery improves people's quality of life by at least a 'very small' amount, 'immediate surgery' would become the preferred option.

Table 38: Specimen base-case incremental cost-effectiveness results for example profile 5, with a 'very small' immediate quality of life benefit ascribed to surgery

| Strategy | Absolute | | Incremental | | |
|--|-----------|-----------------|-------------|-----------------|---------------|
| | Costs (£) | Effects (QALYs) | Costs (£) | Effects (QALYs) | ICER (£/QALY) |
| No surgery | £7,386 | 2.981 | | | |
| Delayed surgery | £8,113 | 3.079 | £727 | 0.098 | £7,432 |
| Immediate surgery | £8,487 | 3.119 | £373 | 0.040 | £9,325 |
| <i>Assuming surgery confers a 'very small' immediate utility gain (0.02)</i> | | | | | |

J.4.3.4 Sensitivity analyses

Faster rate of acuity decline

As with the first eye, results (no full matrix shown) suggest uniformly that, if the BCVA of eyes with cataracts deteriorates at the speed observed by Leinonen and Laatikainen (1999), no immediate improvement in HRQoL is necessary to make surgery cost effective compared with no surgery or delayed surgery, irrespective of the individual's characteristics and ocular risk factors.

Background NHS costs

The results for these sensitivity analyses are similar to those seen for the first eye (see J.4.2.4). Once more, when 'unrelated' costs are included (see J.3.3.19), cataract surgery becomes less cost effective. Full results matrices are provided in Subappendix Jd.

If the 'unrelated' costs are applied to the first postoperative year only (Figure 37, Figure 38), results change for 90-year-olds only. Here, there are multiple scenarios in which an immediate HRQoL benefit of 'very small' magnitude is necessary to make 'immediate surgery' cost effective compared with 'no surgery' or 'delayed surgery', and a small number where a 'small' benefit has to be assumed to achieve the same result (always where BCVA in the cataractous eye is 6/6 and the risk of both PCR and visual loss is high. See Subappendix Jc for illustrative examples of changes in visual function that might meet these definitions.

When the additional costs are assumed to apply in all postoperative years, some degree of immediate HRQoL gain is necessary to counterbalance them and, among 90-year-olds (especially where BCVA is good in both eyes and risk of visual loss is high), the gain would have to be of at least 'moderate' magnitude to make 'immediate surgery' cost effective compared with 'no surgery' or 'delayed surgery' (Figure 39, Figure 40). Again, we emphasise that this is a non-reference-case sensitivity analysis (see J.4.2.4 for discussion).

Alternative – 6/9 – threshold for delayed surgery

In our sensitivity analysis exploring the impact of a 6/9 threshold for delayed surgery, we found that 'immediate surgery' remained optimal in most cases, even if it confers no immediate HRQoL benefit. There are some scenarios among 90-year-olds for which 'delayed (6/9) surgery' represents a better balance of benefits and costs unless it can be assumed that surgery will make a difference to the patient's HRQoL that can be categorised as 'very small'. In all these cases, risk of visual loss is raised and/or BCVA in both eyes is unimpaired. A full results matrix for the second-eye decision-problem is shown in Figure 43 in Subappendix Jd.

Higher costs of cataract surgery

For second eyes, the effect is similar to that observed in first-eyes but in all cases of 90 year olds at any level of risk when acuity is 6/6 in both eyes a “very small” benefit is required. This pattern is also observed in the comparison between immediate and delayed surgery for second eyes.

J.5 Discussion

J.5.1.1 Principal findings

For a large majority of patients with symptomatic cataract, it is clearly optimal to offer surgery, and it is not cost effective to delay this until a VA threshold is met. This is true whether for first- or second-eye surgery. For some combinations of characteristics (typically relating to older patients with a high risk of perioperative visual loss), an expectation of improved quality of life is necessary to make surgery cost effective but, in all such cases, the magnitude of anticipated gain must only of 'very small' to justify immediate surgery.

This model suggests that for the majority of cases delaying surgery until a visual acuity threshold is reached is sub-optimal, will result in a potentially avoidable loss of QALYs, and possibly increase costs by raising the demand for low vision support services, relative to offering immediate surgery. Age is a risk factor for both PCR and visual loss, and therefore delaying surgery is likely to increase risks of poor outcome in older people. This applies in the context of both first and second eyes.

J.5.1.2 Strengths of the analysis

This model represents a means of generating evidence to aid decision makers where previously no similar evidence existed in the literature. The model draws on research carried out on large, directly applicable registry databases and is the first cataract health economic model to employ natural history data to simulate the visual acuity changes in **both** phakic and pseudophakic eyes pre and post-surgery. The model also synthesises resource use and cost data from RCTs, previously conducted economic analyses, NHS Reference Costs, and the input of the guideline committee to produce a very detailed costing of cataract surgery which adds to the robustness of the conclusions.

We were able to use a large published, NHS based, peer-reviewed registry (the RCOphth NOD) to parameterise probabilities of visual loss, and posterior capsular rupture. This is the first time this data has been deployed in a health-economic model of cataract surgery. The NOD is a live dataset so should the multivariate logistic regression models we incorporate be updated and published, our model framework is flexible and could be updated with any new analyses.

We acknowledge the ongoing difficulty of using established HRQoL measures, beyond visual acuity, to quantify both the morbidity caused by cataract and the effectiveness of surgery. We have developed an approach that avoids these complications by instead postulating what magnitude of expected HRQoL gain is necessary, given a variety of premises, for cataract surgery to be cost-effective compared with delayed, or no surgery. We have provided some context for these expected levels of benefit with reference to a newer index of HRQoL, the VFQ-UI. Future research, validating HRQoL measures in populations with cataract, would provide further context for our results.

This model represents the first attempt to evaluate the cost-effectiveness of potential visual acuity thresholds in cataract surgery. One of the central rationales for this model and the prioritising of the relevant review questions for economic analyses was the committee concerns about how cataract could be rationed by imposing visual acuity thresholds for referral where no evidence exists to support their use. This model has explicitly compared strategies of immediate surgery, delayed surgery using two potential thresholds, and a no surgery option. In the majority of iterations the model shows that immediate surgery, whether for first or second eyes, is optimal compared to delaying surgery.

J.5.1.3 Weaknesses of the analysis

Whilst the model structure presents an advantageous departure from the typical engineering of health economic decision models, this is also a weakness as the model does not lend itself to a thoroughgoing sensitivity analysis. Although, the utility of any probabilistic sensitivity analysis in the context of this model structure is debatable. It may be possible to use PSA to describe credible intervals for the utility values populating the result matrices, but these values are already smoothed by the categorisation described in section J.3.4, and it is likely that presenting (and interpreting) such data would be a significant challenge with unclear benefits for the clarity of the conclusions drawn. However, the lack of a concise statistical explanation of the uncertainty in the model, beyond the confidence limits for parameters described in this document and the deterministic sensitivity analyses detailed in section J.3.5, remains a limitation.

It remains a significant challenge to contextualise the HRQoL categories used by the model with reference to specific HRQoL instruments, as all such instruments are flawed when applied to the task of measuring the HRQoL impact of cataract and the effectiveness of surgery in QALY terms. Further work is needed in this regard to help the general quantification of HRQoL in cataract but also to help communicate the results of our model to patients and practitioners by providing realistic vignettes of what a “small” gain in HRQoL for a patient with cataract might mean in terms of survey response.

There is considerable uncertainty in our understanding of how cataract develops over time, what the consequences are in terms of VA and HRQoL, and the rate at which these consequences manifest. Despite an extensive search of the literature, we were forced to rely on two Scandinavian cohort studies to parameterise the visual acuity impacts of cataract and the natural history of phackic/pseudophakic first and fellow-eyes. A complete, unbiased understanding of this problem could only be gained via a large, randomised controlled trial whereby patients are assigned to immediate, delayed or no surgery arms and followed up over regular intervals for the remainder of their life expectancy. For obvious ethical reasons this study will never take place. It is hoped that ophthalmology databases in the NHS setting

may in future contain longer-term follow-up data on pseudophakic eyes and fellow-eyes which will aid in part to addressing this weakness in the richness of data available currently.

J.5.1.4 Comparison with other CUAs

It is clear from previously published economic evaluations that there is variation in the calculated ICERs for first and second-eye surgery, although in all published studies the base-case analyses suggest that surgery is cost-effective at a threshold value of £20,000 per QALY when a lifetime perspective is taken (Table 39). One of the possible reasons for the relatively large ICERs given the low cost of cataract surgery is the use of HRQoL tools such as the EQ-5D which may not have the sensitivity to detect the benefits of surgery. Unlike our model, none of the analyses published to date have attempted to model the decline in visual acuity experienced by people with cataract and have therefore significantly overvalued no-surgery strategies and underestimated the harms of visual loss. In our model, we incorporate additional mortality hazards associated with visual impairment and additional NHS/PSS costs of low vision services, and this combined with the simulation of visual acuity decline means that our model represents a more robust analysis of the consequences of no surgery/delayed surgery strategies than those published before, and more completely reflect the benefits and savings associated with immediate surgery. Our model also improves upon previous analyses by using a large, UK specific database (RCOphth NOD) of cataract surgery outcomes and risk factors for visual loss, rather than a single trial or single centre cohort, which may make our model more directly relevant to the NHS setting.

Table 39 Results of published CUAs for Cataract Surgery

| Study cohort | Context | ICER | Source |
|--|---|--|-------------------------------|
| Hypothetical cohort parameterised from previously published RCTs and economic evaluations. | 2 nd eye vs no surgery. UK setting. | £1,964 | Frampton et al. 2014 |
| Hypothetical cohort based on cataract patients at a single centre | Immediate vs delayed sequential surgery | Immediate bilateral sequential surgery dominated delayed bilateral sequential surgery. | Malvankar-Mehta et al. (2013) |
| 239 women aged ≥ 70 | 2nd eye only. Immediate surgery versus delayed surgery. UK study. | (a) £44,263 (1 year) (b) £17,299 (modelled over life time) | Sach et al. 2010 |
| 306 women aged ≥ 70 | 1st eye. Surgery vs delayed surgery. UK study | (a) £35,704 (1 year) (b) £13,172 (modelled over lifetime) | Sach et al. 2007 |
| 250 patients with low predicted probability of improvement. Immediate surgery vs watchful waiting. | 1st eye. Surgery vs watchful waiting. US study. 6 months horizon. | (a) \$23,750 (overall) (b) \$33,180 (very low probability of improvement) | Naim et al. 2006 |
| 219 patients. | 1st and 2nd eye. Finnish study. Unilateral vs bilateral surgery. | (a) £4,345 (both eyes) (b) £6,959 (one eye) | Rasanen et al. 2006 |

J.6 Conclusions

We present a model of first and second eye cataract surgery comparing immediate, delayed and no surgery treatment options. The model represents a departure from the typically employed economic modelling approaches in NICE Guidelines and the wider literature, but the model results suggest that for the majority of patients presenting for cataract surgery, immediate surgery may be the most cost-effective strategy even if it infers no, or only very small, immediate HRQoL benefit. In the vast majority of modelled situations, delaying surgery until a visual acuity threshold is met is sub-optimal by comparison. These findings are broadly robust to well-defined but limited sensitivity analyses on costs, progression rates, and acuity thresholds which enact small changes to the results as expected but do not substantially change the conclusions drawn from the model.

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Subappendix Jb – Example patient profiles: risk of PCR and visual loss

Jb.1 Risk of PCR and visual loss

For generating results for multiple scenarios (see J.3.4), we classified risk of PCR and risk of visual loss into three categories: low, moderate and high, which we defined as 0.02, 0.06 and 0.15, respectively, for both outcomes. The model is not fundamentally tied to any way of estimating these risks. However, as an example of how they might be derived using the best published data currently available (and to elucidate how we arrived at our broad risk categories), the following sets out some worked examples of calculations.

The best UK-specific estimates of risk of visual loss and PCR available in the literature are those derived from the logistic multiple regression models published by Sparrow et al. (2012) and Narendran et al. (2009). (see J.3.3.3 for details). We defined our risk strata on the basis of absolute risk estimates generated by iteratively including/excluding variables in these models. This was done by first developing exemplar profiles with the lowest (no risk factors) and highest possible (all risk factors) predictive probabilities of PCR and visual loss, and then observing the changes in probability between these extremes as risk factors are added or removed from the model. Because these covariates are on logistic scales, the absolute risks of PCR and visual loss in low-risk and moderate-risk categories are much lower than some possible values of absolute risk for those profiles with many risk factors included. This is reflected in the midpoints adopted for low / moderate / high probability of PCR and visual loss which are set at 0.02 / 0.06 / 0.15 for both. Some examples are given here to illustrate those levels of risk.

In Table 40, the profile describes a patient of 60 years of age, with no additional comorbidities or risk factors other than medium-sized pupils. The probability of PCR and visual loss in this example falls below the threshold for low risk (0.02).

Table 40: Exemplar profile – low risk of PCR and low risk of visual loss

| Variable | Value | PCR | Visual loss |
|-------------------------------------|--------------------|-----------------------------------|-----------------------------------|
| Constant term (odds scale) | | 0.00742 | 0.00727 |
| Odds ratios for risk factors | | | |
| Sex | Female | 1 | n/a |
| Age | 60 | 1 | 1 |
| Glaucoma | No | 1 | n/a |
| Diabetic retinopathy | No | 1 | 1 |
| Any other ocular comorbidity | No | n/a | 1 |
| Brunescent / white cataract | No | 1 | n/a |
| No fundal view / vitreous opacities | No | 1 | n/a |
| Pseudoexfoliation / phacodonesis | No | 1 | n/a |
| Pupil size | Medium (5.6-6.4mm) | 1 | 0.78 |
| Axial length | ≥26.00 | 1.47 | 0.77 |
| Doxazosin | No | 1 | n/a |
| Able to lie flat | Yes | 1 | n/a |
| Calculated probability | | | |
| | | 0.019 (Low risk) | 0.006 (Low risk) |

Table 41 details a 70 year old patient with some comorbidities and an inability to lie flat during the cataract surgery. This combination of factors increases the probability of PCR to moderate, whilst the probability of visual loss is increased but remains low.

Table 41: Exemplar profile – moderate risk of PCR with low risk of visual loss

| Variable | Value | PCR | Visual loss |
|-------------------------------------|--------------------|----------------------------|----------------------------|
| Constant term (odds scale) | | 0.00742 | 0.00727 |
| Odds ratios for risk factors | | | |
| Sex | Female | 1 | n/a |
| Age | 70 | 1.42 | 1.08 |
| Glaucoma | No | 1 | n/a |
| Diabetic retinopathy | No | 1 | 1 |
| Any other ocular comorbidity | Yes | n/a | 2.28 |
| Brunescent / white cataract | No | 1 | n/a |
| No fundal view / vitreous opacities | No | 1 | n/a |
| Pseudoexfoliation / phacodonesis | Yes | 2.92 | n/a |
| Pupil size | Medium (5.6-6.4mm) | 1.14 | 0.78 |
| Axial length | ≥26.00 | 1.47 | 0.77 |
| Doxazosin | No | 1 | n/a |
| Able to lie flat | No | 1.27 | n/a |
| Calculated probability | | | |
| | | 0.061 (Low risk) | 0.014 (Low risk) |

Table 42 describes an exemplar case of 80yrs of age, with glaucoma and diabetes, a brunescent or white cataract which is more difficult to perform phacoemulsification on, large pupils, shorter axial length, is taking beta-blockers and cannot lie flat for the surgery. In this case the risk of PCR as evaluated by the model is described as high, and the corresponding likelihood of poor visual outcome is categorised as moderate.

Table 42: Exemplar profile – high risk of PCR with moderate risk of visual loss

| Variable | Value | PCR | Visual loss |
|-------------------------------------|----------------|-----------------------------|---------------------------------|
| Constant term (odds scale) | | 0.00742 | 0.00727 |
| Odds ratios for risk factors | | | |
| Sex | Male | 1.28 | n/a |
| Age | 80 | 1.58 | 1.36 |
| Glaucoma | Yes | 1.3 | n/a |
| Diabetic retinopathy | Yes | 1.63 | 1.73 |
| Any other ocular comorbidity | Yes | n/a | 2.28 |
| Brunescent / white cataract | Yes | 1 | n/a |
| No fundal view / vitreous opacities | No | 1 | n/a |
| Pseudoexfoliation / phacodonesis | No | 2.92 | n/a |
| Pupil size | Large (>6.5mm) | 1 | 1 |
| Axial length | ≤22.37 | 1 | 1.51 |
| Doxazosin | Yes | 1.51 | n/a |
| Able to lie flat | No | 1.27 | n/a |
| Calculated probability | | | |
| | | 0.154 (High risk) | 0.086 (Moderate risk) |

Table 43 describes a patient profile with all possible comorbidities, and other risk factors at the worst possible level (small pupils, short axial length, unable to lie flat and taking beta blockers). This results in a high risk of both PCR and visual loss.

Table 43: Exemplar profile – high risk of PCR and high risk of visual loss

| Variable | Value | PCR | Visual loss |
|-------------------------------------|----------------|------------------------------------|--|
| Constant term (odds scale) | | 0.00742 | 0.00727 |
| Odds ratios for risk factors | | | |
| Sex | Male | 1.28 | n/a |
| Age | 90 | 2.37 | 1.93 |
| Glaucoma | Yes | 1.3 | n/a |
| Diabetic retinopathy | Yes | 1.63 | 1.73 |
| Any other ocular comorbidity | Yes | n/a | 2.28 |
| Brunescent / white cataract | Yes | 2.99 | n/a |
| No fundal view / vitreous opacities | Yes | 2.46 | n/a |
| Pseudoexfoliation / phacodonesis | Yes | 2.92 | n/a |
| Pupil size | Small (<5.5mm) | 1.45 | 1.85 |
| Axial length | ≤22.37 | 1 | 1.51 |
| Doxazosin | Yes | 1.51 | n/a |
| Able to lie flat | No | 1.27 | n/a |
| Calculated probability | | | |
| | | 0.740 (High risk) | 0.383 (Moderate risk) |

Formulae for calculating the probability of PCR:

$$O_{PCR} = x \prod OR_{PCR}$$

$$P_{PCR} = \frac{O_{PCR}}{1 + O_{PCR}}$$

Where:

O_{PCR} = odds of PCR

OR_{PCR} = odds ratios for risk factors

x = Constant term (intercept from risk of PCR model [odds on natural scale])

P_{PCR} = probability of PCR

Formulae for calculating probability of visual loss:

$$O_{VL|noPCR} = y \prod OR_{VL}$$

$$P_{VL|noPCR} = \frac{O_{VL|noPCR}}{1 + O_{VL|noPCR}}$$

$$O_{VL|PCR} = OR_{PCR} y \prod OR_{VL}$$

$$P_{VL|PCR} = \frac{O_{VL|PCR}}{1 + O_{VL|PCR}}$$

$$P_{VL} = P_{PCR} P_{VL|PCR} + (1 - P_{PCR}) P_{VL|noPCR}$$

Where:

$O_{VL|noPCR}$ = Odds of visual loss given no PCR

$O_{VL|PCR}$ = Odds of visual loss given PCR

OR_{PCR} = Odds ratio for visual loss given PCR (=5.74)

y = Constant term (intercept from risk of visual loss model [odds on natural scale])

O_{VL} = Odds of visual loss

$P_{VL|PCR}$ = Probability of visual loss given PCR

$P_{VL|noPCR}$ = Probability of visual loss given no PCR

Subappendix Jc – Example patient profiles: change in quality of life

In section J.3.3.24 we discuss some of the challenges of quantifying baseline HRQoL in people with cataract and the associated difficulty in reliably capturing the effectiveness of cataract removal when using commonly applied HRQoL instruments such as EQ-5D. For baseline HRQoL, we use natural breaks to characterise low, moderate and good categories as 0.4/ 0.6/ 0.8. For utility gains, we started with the EQ-5D as a template and developed the following categories accordingly:

- A **very small** change is any change less than moving a full category (i.e. less than the EQ-5D can measure in an individual case)
- A **small** change is less than the smallest change possible when moving from a level 3 to a level 2, but greater than the smallest change possible when changing from a level 2 to a level 1
- A **moderate** change is greater than this but less than the smallest change possible when either:
 - a) moving from a 3 → 1OR
 - b) moving from 2 → 1 in at least TWO separate categories.
- A **large** change is any change larger than this

These criteria equate to utility ranges of:

- Very Small = 0.00–0.03
- Small = 0.03–0.06
- Moderate = 0.06–0.10
- Large = >0.10

These can be applied to any index. The recently developed VFQ-UI – which has a societal preference valuation like the EQ-5D, meaning it can be used to generate QALYs in cost–utility analyses – is one option that addresses some of the challenges inherent in estimating the impact of visual impairment of HRQoL. Tables Jc.1–Jc.4 illustrate baseline and post-cataract surgery HRQoL scenarios corresponding to our categorisation of HRQoL scores (low, moderate, good at baseline and very small, small, moderate and large gains post-surgery) side-by-side using the VFQ-UI.

Jc.1 Very small

| VFQ _{UI} Dimension | Pre-Surgery Scenario | Post-Surgery Scenario |
|---|--|--|
| How much difficulty do you have doing work or hobbies that require you to see well up close, such as cooking, sewing, fixing things around the house, or using hand tools? Would you say: | <i>Stopped doing this because of your eyesight</i> | <i>Extreme Difficulty</i> |
| Because of your eyesight, how much difficulty do you have seeing how people react to things you say? | <i>Stopped doing this because of your eyesight</i> | <i>Stopped doing this because of your eyesight</i> |
| Because of your eyesight, how much difficulty do you have going out to see movies, plays, or sports events? | <i>Stopped doing this because of your eyesight</i> | <i>Stopped doing this because of your eyesight</i> |
| Are you limited in how long you can work or do other activities because of your vision? | <i>All of the time</i> | <i>All of the time</i> |
| I stay home most of the time because of my eyesight. | <i>Definitely True</i> | <i>Definitely True</i> |
| I worry about doing things that will embarrass myself or others, because of my eyesight | <i>Definitely True</i> | <i>Definitely True</i> |

Figure 22: Example of a change in VFQ-UI response corresponding to a very small gain (Δ of 0.016) in utility

Jc.2 Small

| VFQ _{UI} Dimension | Pre-Surgery Scenario | Post-Surgery Scenario |
|---|--|--|
| How much difficulty do you have doing work or hobbies that require you to see well up close, such as cooking, sewing, fixing things around the house, or using hand tools? Would you say: | <i>Stopped doing this because of your eyesight</i> | <i>Extreme Difficulty</i> |
| Because of your eyesight, how much difficulty do you have seeing how people react to things you say? | <i>Stopped doing this because of your eyesight</i> | <i>Stopped doing this because of your eyesight</i> |
| Because of your eyesight, how much difficulty do you have going out to see movies, plays, or sports events? | <i>Stopped doing this because of your eyesight</i> | <i>Stopped doing this because of your eyesight</i> |
| Are you limited in how long you can work or do other activities because of your vision? | <i>All of the time</i> | <i>A little of the time</i> |
| I stay home most of the time because of my eyesight. | <i>Definitely True</i> | <i>Definitely True</i> |
| I worry about doing things that will embarrass myself or others, because of my eyesight | <i>Definitely True</i> | <i>Definitely True</i> |

Figure 23: Example of a change in VFQ-UI response corresponding to a small gain (Δ of 0.044) in utility

Jc.3 Moderate

| VFQ _{UI} Dimension | Pre-Surgery Scenario | Post-Surgery Scenario |
|---|--|----------------------------|
| How much difficulty do you have doing work or hobbies that require you to see well up close, such as cooking, sewing, fixing things around the house, or using hand tools? Would you say: | <i>Stopped doing this because of your eyesight</i> | <i>Extreme difficulty</i> |
| Because of your eyesight, how much difficulty do you have seeing how people react to things you say? | <i>A little difficulty</i> | <i>Moderate difficulty</i> |
| Because of your eyesight, how much difficulty do you have going out to see movies, plays, or sports events? | <i>A little difficulty</i> | <i>A little difficulty</i> |
| Are you limited in how long you can work or do other activities because of your vision? | <i>None of the time</i> | <i>None of the time</i> |
| I stay home most of the time because of my eyesight. | <i>Definitely true</i> | <i>Mostly true</i> |
| I worry about doing things that will embarrass myself or others, because of my eyesight | <i>Definitely true</i> | <i>Mostly true</i> |

Figure 24: Example of a change in VFQ-UI response corresponding to a moderate gain (Δ of 0.078) in utility

Jc.4 Large

| VFQ _{UI} Dimension | Pre-Surgery Scenario | Post-Surgery Scenario |
|---|-----------------------------|-----------------------------|
| How much difficulty do you have doing work or hobbies that require you to see well up close, such as cooking, sewing, fixing things around the house, or using hand tools? Would you say: | <i>Moderate difficulty</i> | <i>No difficulty at all</i> |
| Because of your eyesight, how much difficulty do you have seeing how people react to things you say? | <i>Moderate difficulty</i> | <i>No difficulty at all</i> |
| Because of your eyesight, how much difficulty do you have going out to see movies, plays, or sports events? | <i>Moderate difficulty</i> | <i>No difficulty at all</i> |
| Are you limited in how long you can work or do other activities because of your vision? | <i>A little of the time</i> | <i>None of the time</i> |
| I stay home most of the time because of my eyesight. | <i>Definitely false</i> | <i>Definitely false</i> |
| I worry about doing things that will embarrass myself or others, because of my eyesight | <i>Definitely false</i> | <i>Definitely false</i> |

Figure 25: Example of a change in VFQ-UI response corresponding to a large gain (Δ of 0.175) in utility

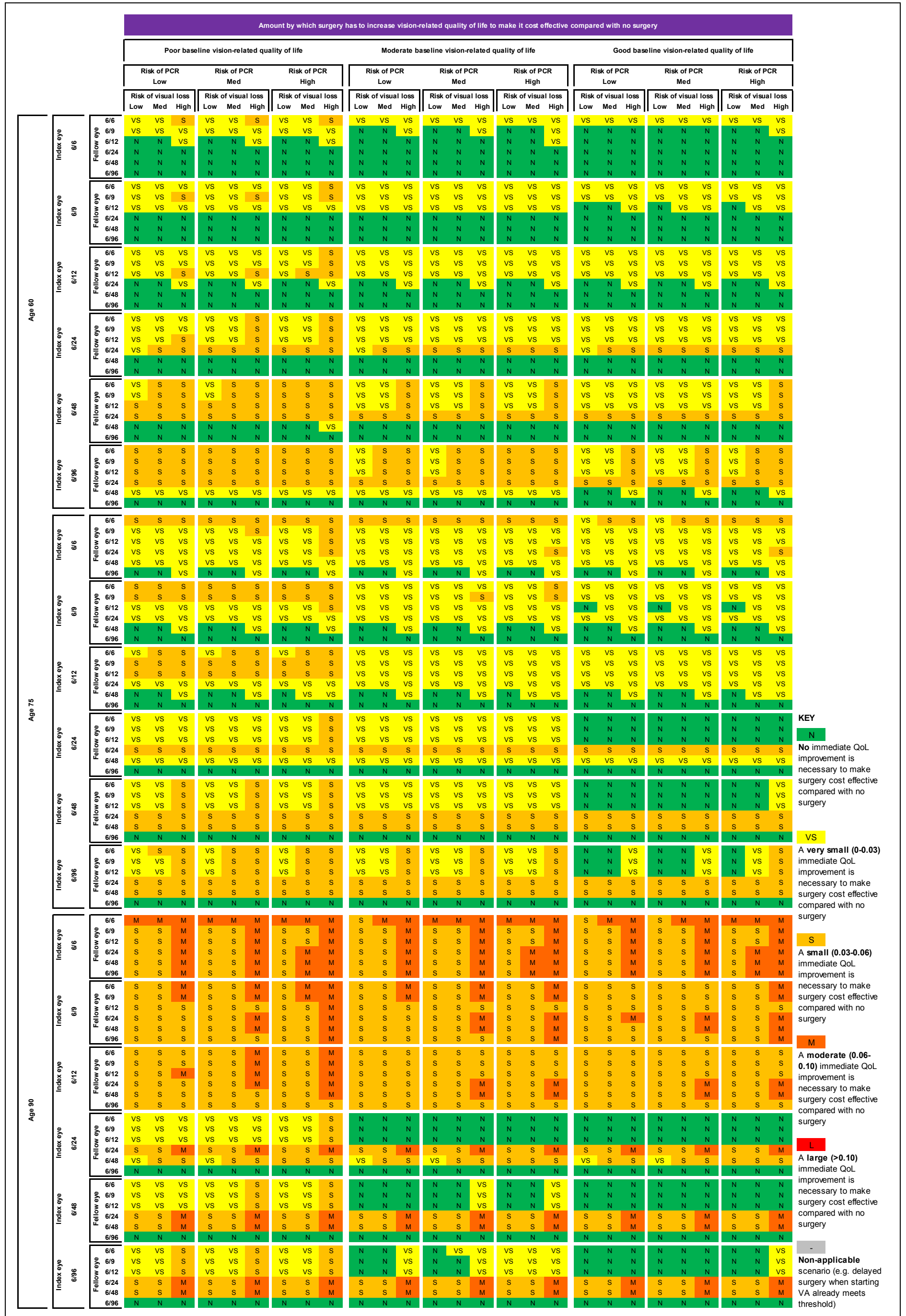
Subappendix Jd – Cost effectiveness model – results (full matrices)

| | | Amount by which surgery has to increase vision-related quality of life to make it cost effective compared with no surgery | | | | | | | | | | | | | | | | | | | | | | | | | | | |
|--------|----------------|---|---|---|----------------------------------|---|---|----------------------------------|---|---|--|---|---|----------------------------------|---|---|----------------------------------|---|---|--|---|---|----------------------------------|---|---|----------------------------------|---|---|----|
| | | Poor baseline vision-related quality of life | | | | | | | | | Moderate baseline vision-related quality of life | | | | | | | | | Good baseline vision-related quality of life | | | | | | | | | |
| | | Risk of PCR Low | | | Risk of PCR Med | | | Risk of PCR High | | | Risk of PCR Low | | | Risk of PCR Med | | | Risk of PCR High | | | Risk of PCR Low | | | Risk of PCR Med | | | Risk of PCR High | | | |
| | | Risk of visual loss Low Med High | | | Risk of visual loss Low Med High | | | Risk of visual loss Low Med High | | | Risk of visual loss Low Med High | | | Risk of visual loss Low Med High | | | Risk of visual loss Low Med High | | | Risk of visual loss Low Med High | | | Risk of visual loss Low Med High | | | Risk of visual loss Low Med High | | | |
| Age 60 | Index eye 6/6 | Fellow eye 6/6 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N |
| | | Fellow eye 6/9 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N |
| | | Fellow eye 6/12 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N |
| | Index eye 6/9 | Fellow eye 6/9 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N |
| | | Fellow eye 6/12 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N |
| | | Fellow eye 6/24 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N |
| | Index eye 6/12 | Fellow eye 6/12 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N |
| | | Fellow eye 6/24 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N |
| | | Fellow eye 6/48 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N |
| | Index eye 6/24 | Fellow eye 6/24 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N |
| | | Fellow eye 6/48 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N |
| | | Fellow eye 6/96 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N |
| | Index eye 6/48 | Fellow eye 6/48 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N |
| | | Fellow eye 6/96 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N |
| | | Fellow eye 6/192 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N |
| | Index eye 6/96 | Fellow eye 6/96 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N |
| | | Fellow eye 6/192 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N |
| | | Fellow eye 6/384 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N |
| Age 75 | Index eye 6/6 | Fellow eye 6/6 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N |
| | | Fellow eye 6/9 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N |
| | | Fellow eye 6/12 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N |
| | Index eye 6/9 | Fellow eye 6/9 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N |
| | | Fellow eye 6/12 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N |
| | | Fellow eye 6/24 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N |
| | Index eye 6/12 | Fellow eye 6/12 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N |
| | | Fellow eye 6/24 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N |
| | | Fellow eye 6/48 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N |
| | Index eye 6/24 | Fellow eye 6/24 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N |
| | | Fellow eye 6/48 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N |
| | | Fellow eye 6/96 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N |
| | Index eye 6/48 | Fellow eye 6/48 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N |
| | | Fellow eye 6/96 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N |
| | | Fellow eye 6/192 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N |
| | Index eye 6/96 | Fellow eye 6/96 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N |
| | | Fellow eye 6/192 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N |
| | | Fellow eye 6/384 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N |
| Age 90 | Index eye 6/6 | Fellow eye 6/6 | N | N | VS | N | N | VS | N | N | VS | N | N | VS | N | N | VS | N | N | VS | N | N | VS | N | N | VS | N | N | VS |
| | | Fellow eye 6/9 | N | N | N | N | N | VS | N | N | VS | N | N | VS | N | N | VS | N | N | VS | N | N | VS | N | N | VS | N | N | VS |
| | | Fellow eye 6/12 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N |
| | Index eye 6/9 | Fellow eye 6/9 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N |
| | | Fellow eye 6/12 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N |
| | | Fellow eye 6/24 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N |
| | Index eye 6/12 | Fellow eye 6/12 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N |
| | | Fellow eye 6/24 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N |
| | | Fellow eye 6/48 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N |
| | Index eye 6/24 | Fellow eye 6/24 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N |
| | | Fellow eye 6/48 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N |
| | | Fellow eye 6/96 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N |
| | Index eye 6/48 | Fellow eye 6/48 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N |
| | | Fellow eye 6/96 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N |
| | | Fellow eye 6/192 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N |
| | Index eye 6/96 | Fellow eye 6/96 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N |
| | | Fellow eye 6/192 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N |
| | | Fellow eye 6/384 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N |

KEY

- N** No immediate QoL improvement is necessary to make surgery cost effective compared with no surgery
- VS** A very small (0-0.03) immediate QoL improvement is necessary to make surgery cost effective compared with no surgery
- S** A small (0.03-0.06) immediate QoL improvement is necessary to make surgery cost effective compared with no surgery
- M** A moderate (0.06-0.10) immediate QoL improvement is necessary to make surgery cost effective compared with no surgery
- L** A large (>0.10) immediate QoL improvement is necessary to make surgery cost effective compared with no surgery
- Non-applicable scenario (e.g. delayed surgery when starting VA already meets threshold)

Figure 34: Sensitivity analysis (cost of cataract surgery increased by £500) – results matrix – first-eye immediate -v- no surgery



KEY

- N** No immediate QoL improvement is necessary to make surgery cost effective compared with no surgery
- VS** A very small (0-0.03) immediate QoL improvement is necessary to make surgery cost effective compared with no surgery
- S** A small (0.03-0.06) immediate QoL improvement is necessary to make surgery cost effective compared with no surgery
- M** A moderate (0.06-0.10) immediate QoL improvement is necessary to make surgery cost effective compared with no surgery
- L** A large (>0.10) immediate QoL improvement is necessary to make surgery cost effective compared with no surgery
- Non-applicable scenario (e.g. delayed surgery when starting VA already meets threshold)

Figure 39: Sensitivity analysis (unrelated future costs, all years) – results matrix – second-eye immediate -v- no surgery

| | | Amount by which immediate surgery has to increase vision-related quality of life to make it cost effective compared with waiting until the index eye reaches 6/12 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
|--------|----------------|---|----|----|----------------------------------|----|----|----------------------------------|----|----|--|----|----|----------------------------------|----|----|----------------------------------|----|----|--|----|----|----------------------------------|----|----|----------------------------------|----|----|----|----|----|----|
| | | Poor baseline vision-related quality of life | | | | | | | | | Moderate baseline vision-related quality of life | | | | | | | | | Good baseline vision-related quality of life | | | | | | | | | | | | |
| | | Risk of PCR Low | | | Risk of PCR Med | | | Risk of PCR High | | | Risk of PCR Low | | | Risk of PCR Med | | | Risk of PCR High | | | Risk of PCR Low | | | Risk of PCR Med | | | Risk of PCR High | | | | | | |
| | | Risk of visual loss Low Med High | | | Risk of visual loss Low Med High | | | Risk of visual loss Low Med High | | | Risk of visual loss Low Med High | | | Risk of visual loss Low Med High | | | Risk of visual loss Low Med High | | | Risk of visual loss Low Med High | | | Risk of visual loss Low Med High | | | Risk of visual loss Low Med High | | | | | | |
| Age 60 | Index eye 6/6 | Fellow eye 6/6 | VS | VS | S | VS | VS | S | VS | VS | S | VS | VS | S | VS | VS | S | VS | VS | S | VS | VS | S | VS | VS | S | VS | VS | S | VS | VS | S |
| | | Fellow eye 6/9 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N |
| | | Fellow eye 6/12 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N |
| | Index eye 6/9 | Fellow eye 6/6 | VS | VS | VS | VS | VS | VS | VS | VS | VS | VS | VS | VS | VS | VS | VS | VS | VS | VS | VS | VS | VS | VS | VS | VS | VS | VS | VS | VS | VS | VS |
| | | Fellow eye 6/9 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N |
| | | Fellow eye 6/12 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N |
| | Index eye 6/12 | Fellow eye 6/6 | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - |
| | | Fellow eye 6/9 | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - |
| | | Fellow eye 6/12 | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - |
| | Index eye 6/24 | Fellow eye 6/6 | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - |
| | | Fellow eye 6/9 | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - |
| | | Fellow eye 6/12 | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - |
| | Index eye 6/48 | Fellow eye 6/6 | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - |
| | | Fellow eye 6/9 | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - |
| | | Fellow eye 6/12 | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - |
| | Index eye 6/96 | Fellow eye 6/6 | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - |
| | | Fellow eye 6/9 | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - |
| | | Fellow eye 6/12 | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - |
| Age 75 | Index eye 6/6 | Fellow eye 6/6 | S | S | S | S | S | S | S | S | S | S | S | S | S | S | S | S | S | S | S | S | S | S | S | S | S | S | S | S | S | S |
| | | Fellow eye 6/9 | N | VS | VS | N | VS | VS | VS | VS | VS | N | VS | VS | N | VS | VS | VS | VS | VS | N | VS | VS | N | VS | VS | VS | VS | VS | VS | VS | VS |
| | | Fellow eye 6/12 | N | N | VS | N | N | VS | N | N | VS | N | N | VS | N | N | VS | N | N | VS | N | N | VS | N | N | VS | N | N | VS | N | N | VS |
| | Index eye 6/9 | Fellow eye 6/6 | S | S | S | S | S | S | S | S | S | S | S | S | S | S | S | S | S | S | S | S | S | S | S | S | S | S | S | S | S | S |
| | | Fellow eye 6/9 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N |
| | | Fellow eye 6/12 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N |
| | Index eye 6/12 | Fellow eye 6/6 | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - |
| | | Fellow eye 6/9 | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - |
| | | Fellow eye 6/12 | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - |
| | Index eye 6/24 | Fellow eye 6/6 | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - |
| | | Fellow eye 6/9 | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - |
| | | Fellow eye 6/12 | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - |
| | Index eye 6/48 | Fellow eye 6/6 | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - |
| | | Fellow eye 6/9 | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - |
| | | Fellow eye 6/12 | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - |
| | Index eye 6/96 | Fellow eye 6/6 | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - |
| | | Fellow eye 6/9 | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - |
| | | Fellow eye 6/12 | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - |
| Age 90 | Index eye 6/6 | Fellow eye 6/6 | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M | M |
| | | Fellow eye 6/9 | S | S | M | S | S | M | S | S | M | S | S | M | S | S | M | S | S | M | S | S | M | S | S | M | S | S | M | S | S | M |
| | | Fellow eye 6/12 | S | S | M | S | S | M | S | S | M | S | S | M | S | S | M | S | S | M | S | S | M | S | S | M | S | S | M | S | S | M |
| | Index eye 6/9 | Fellow eye 6/6 | S | S | M | S | S | M | S | S | M | S | S | M | S | S | M | S | S | M | S | S | M | S | S | M | S | S | M | S | S | M |
| | | Fellow eye 6/9 | VS | VS | S | VS | VS | S | VS | VS | S | VS | VS | S | VS | VS | S | VS | VS | S | VS | VS | S | VS | VS | S | VS | VS | S | VS | VS | S |
| | | Fellow eye 6/12 | S | S | S | S | S | S | S | S | S | S | S | S | S | S | S | S | S | S | S | S | S | S | S | S | S | S | S | S | S | S |
| | Index eye 6/12 | Fellow eye 6/6 | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - |
| | | Fellow eye 6/9 | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - |
| | | Fellow eye 6/12 | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - |
| | Index eye 6/24 | Fellow eye 6/6 | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - |
| | | Fellow eye 6/9 | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - |
| | | Fellow eye 6/12 | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - |
| | Index eye 6/48 | Fellow eye 6/6 | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - |
| | | Fellow eye 6/9 | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - |
| | | Fellow eye 6/12 | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - |
| | Index eye 6/96 | Fellow eye 6/6 | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - |
| | | Fellow eye 6/9 | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - |
| | | Fellow eye 6/12 | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - |

KEY

- N** No immediate QoL improvement is necessary to make surgery cost effective compared with delayed surgery
- VS** A very small (0-0.03) immediate QoL improvement is necessary to make surgery cost effective compared with delayed surgery
- S** A small (0.03-0.06) immediate QoL improvement is necessary to make surgery cost effective compared with delayed surgery
- M** A moderate (0.06-0.10) immediate QoL improvement is necessary to make surgery cost effective compared with delayed surgery
- L** A large (>0.10) immediate QoL improvement is necessary to make surgery cost effective compared with delayed surgery
- Non-applicable scenario (e.g. delayed surgery when starting VA already meets threshold)

Figure 40: Sensitivity analysis (unrelated future costs, all years) – results matrix – second-eye immediate -v- delayed surgery (threshold 6/12)

| | | Amount by which surgery has to increase vision-related quality of life to make it cost effective compared with no surgery | | | | | | | | | | | | | | | | | | | | | | | | | | | |
|--------|----------------|---|----|----|----------------------------------|----|----|----------------------------------|----|----|--|----|----|----------------------------------|----|----|----------------------------------|----|----|--|----|----|----------------------------------|----|----|----------------------------------|----|----|----|
| | | Poor baseline vision-related quality of life | | | | | | | | | Moderate baseline vision-related quality of life | | | | | | | | | Good baseline vision-related quality of life | | | | | | | | | |
| | | Risk of PCR Low | | | Risk of PCR Med | | | Risk of PCR High | | | Risk of PCR Low | | | Risk of PCR Med | | | Risk of PCR High | | | Risk of PCR Low | | | Risk of PCR Med | | | Risk of PCR High | | | |
| | | Risk of visual loss Low Med High | | | Risk of visual loss Low Med High | | | Risk of visual loss Low Med High | | | Risk of visual loss Low Med High | | | Risk of visual loss Low Med High | | | Risk of visual loss Low Med High | | | Risk of visual loss Low Med High | | | Risk of visual loss Low Med High | | | Risk of visual loss Low Med High | | | |
| Age 60 | Index eye 6/6 | Fellow eye 6/6 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N |
| | | Fellow eye 6/9 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N |
| | | Fellow eye 6/12 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N |
| | Index eye 6/9 | Fellow eye 6/9 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N |
| | | Fellow eye 6/12 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N |
| | | Fellow eye 6/24 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N |
| | Index eye 6/12 | Fellow eye 6/12 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N |
| | | Fellow eye 6/24 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N |
| | | Fellow eye 6/48 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N |
| | Index eye 6/24 | Fellow eye 6/24 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N |
| | | Fellow eye 6/48 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N |
| | | Fellow eye 6/96 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N |
| | Index eye 6/48 | Fellow eye 6/48 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N |
| | | Fellow eye 6/96 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N |
| | | Fellow eye 6/96 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N |
| | Index eye 6/96 | Fellow eye 6/96 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N |
| | | Fellow eye 6/96 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N |
| | | Fellow eye 6/96 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N |
| Age 75 | Index eye 6/6 | Fellow eye 6/6 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N |
| | | Fellow eye 6/9 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N |
| | | Fellow eye 6/12 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N |
| | Index eye 6/9 | Fellow eye 6/9 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N |
| | | Fellow eye 6/12 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N |
| | | Fellow eye 6/24 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N |
| | Index eye 6/12 | Fellow eye 6/12 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N |
| | | Fellow eye 6/24 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N |
| | | Fellow eye 6/48 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N |
| | Index eye 6/24 | Fellow eye 6/24 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N |
| | | Fellow eye 6/48 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N |
| | | Fellow eye 6/96 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N |
| | Index eye 6/48 | Fellow eye 6/48 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N |
| | | Fellow eye 6/96 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N |
| | | Fellow eye 6/96 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N |
| | Index eye 6/96 | Fellow eye 6/96 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N |
| | | Fellow eye 6/96 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N |
| | | Fellow eye 6/96 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N |
| Age 90 | Index eye 6/6 | Fellow eye 6/6 | VS | VS | VS | VS | VS | VS | VS | VS | VS | VS | VS | VS | VS | VS | VS | VS | VS | VS | VS | VS | VS | VS | VS | VS | VS | VS | VS |
| | | Fellow eye 6/9 | N | N | VS | N | N | VS | N | N | VS | N | N | VS | N | N | VS | N | N | VS | N | N | VS | N | N | VS | N | N | VS |
| | | Fellow eye 6/12 | N | N | VS | N | N | VS | N | N | VS | N | N | VS | N | N | VS | N | N | VS | N | N | VS | N | N | VS | N | N | VS |
| | Index eye 6/9 | Fellow eye 6/9 | VS | VS | VS | VS | VS | VS | VS | VS | VS | N | N | VS | N | N | VS | N | N | VS | N | N | VS | N | N | VS | N | N | VS |
| | | Fellow eye 6/12 | N | N | VS | N | N | VS | N | N | VS | N | N | VS | N | N | VS | N | N | VS | N | N | VS | N | N | VS | N | N | VS |
| | | Fellow eye 6/24 | N | N | VS | N | N | VS | N | N | VS | N | N | VS | N | N | VS | N | N | VS | N | N | VS | N | N | VS | N | N | VS |
| | Index eye 6/12 | Fellow eye 6/12 | N | N | VS | N | N | VS | N | N | VS | N | N | VS | N | N | VS | N | N | VS | N | N | VS | N | N | VS | N | N | VS |
| | | Fellow eye 6/24 | N | N | VS | N | N | VS | N | N | VS | N | N | VS | N | N | VS | N | N | VS | N | N | VS | N | N | VS | N | N | VS |
| | | Fellow eye 6/48 | N | N | VS | N | N | VS | N | N | VS | N | N | VS | N | N | VS | N | N | VS | N | N | VS | N | N | VS | N | N | VS |
| | Index eye 6/24 | Fellow eye 6/24 | VS | VS | VS | VS | VS | VS | VS | VS | VS | N | N | VS | N | N | VS | N | N | VS | N | N | VS | N | N | VS | N | N | VS |
| | | Fellow eye 6/48 | VS | VS | VS | VS | VS | VS | VS | VS | VS | N | N | VS | N | N | VS | N | N | VS | N | N | VS | N | N | VS | N | N | VS |
| | | Fellow eye 6/96 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N |
| | Index eye 6/48 | Fellow eye 6/48 | VS | VS | VS | VS | VS | VS | VS | VS | VS | N | N | VS | N | N | VS | N | N | VS | N | N | VS | N | N | VS | N | N | VS |
| | | Fellow eye 6/96 | VS | VS | VS | VS | VS | VS | VS | VS | VS | N | N | VS | N | N | VS | N | N | VS | N | N | VS | N | N | VS | N | N | VS |
| | | Fellow eye 6/96 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N |
| | Index eye 6/96 | Fellow eye 6/96 | VS | VS | VS | VS | VS | VS | VS | VS | VS | N | N | VS | N | N | VS | N | N | VS | N | N | VS | N | N | VS | N | N | VS |
| | | Fellow eye 6/96 | VS | VS | VS | VS | VS | VS | VS | VS | VS | N | N | VS | N | N | VS | N | N | VS | N | N | VS | N | N | VS | N | N | VS |
| | | Fellow eye 6/96 | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N | N |

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Figure 41: Sensitivity analysis (cost of cataract surgery increased by £500) – results matrix – second-eye immediate -v- no surgery

