

# 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).

38 **J.2.2 RQ 3: What are the indicators for referral for cataract surgery & RQ4: What are**  
39 **the optimal clinical thresholds in terms of severity and impairment for referral**  
40 **for cataract surgery**

41 **Naeim et al. (2007)**

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

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

- 52 • for every decade over 65 years, patients receive 1 point;
- 53 • 2 points are added if there is evidence of diabetes mellitus (regardless of the presence of  
54 retinopathy);
- 55 • 1 point is subtracted if the patient has preoperative evidence of a posterior sub-capsular  
56 cataract;
- 57 • 2 points are added if there is evidence of macular degeneration;
- 58 • Preoperative ADVS (Activities of Daily Vision Score) score (range 0-100) multiplied by 0.1  
59 is added to the total score

60 Patients with a CSI score of 10 points or more are considered to have a low probability  
61 (<30%) of improving with surgery.

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

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

77 **Rasanen et al. (2006)**

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

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

93 **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

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

Table 2: Economic evidence tables RQ 3 &amp; 4

Study, Population, Comparators, Quality	Data Sources	Other Comments	Disaggregated			Conclusions	Uncertainty
			Cost	Effect	Cost/QALY		
<b>Naeim et al. (2007) USA</b> 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.  <b>Partially applicable</b> <sup>(a)</sup>  <b>Serious Limitations</b> <sup>(b, c, d)</sup> :	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><b>Rasanen et al. (2006)</b> 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><b>Partially applicable</b> <sup>a</sup></p> <p><b>Serious limitations</b> 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>	<p>Mean €971.00</p>	<p>0.2859</p>	<p>€ 3,396.29</p>	<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. 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"> <li>– Only reported dimension to improve post surgery = vision</li> <li>– Does not match other studies eg VFQ-25, VF-14, HUI-3 multidimensional improvements.</li> </ul>							

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

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

$$120 \quad y = -0.04792x^3 + 0.191x^2 - 0.4233x + 0.9128$$

121  $y = \text{utility}$

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

123 The authors used data on the effectiveness of phacoemulsification taken from the Swedish  
 124 National Cataract Registry, a multicentre prospective trial (Hahn et al. 2010) and a large  
 125 cohort study from a tertiary centre in Germany (Hoffman et al. 2011). In the absence of any  
 126 equivalent evidence on laser-assisted surgery, the model assumed that the benefit of  
 127 femtosecond surgery would be a 5% improvement in the number of eyes achieving ~6/12  
 128 visual acuity post-surgery. The increase in BCVA after cataract surgery in the laser group  
 129 was assumed to reflect improved refraction owing to improved lens positioning as a result of  
 130 more regular capsulotomy incisions, as well as a decrease in the intraoperative complication  
 131 rate. Based on the simulated complication rates of standard and laser-assisted surgery and  
 132 assuming visual acuity improvement of 5% in uncomplicated cases, laser-assisted surgery  
 133 was associated with QALY gains of 0.06, but was also found to have increased costs, with a  
 134 resulting ICER of \$AUS92,862 per QALY gained, which is above conventional thresholds of  
 135 cost effectiveness. Multivariable sensitivity analyses revealed that laser-assisted surgery  
 136 would need to significantly improve visual outcomes and complications rates over standard  
 137 surgery, along with a reduction in cost to patient, to improve cost effectiveness. Modelling a  
 138 best-case scenario of laser-assisted surgery with excellent visual outcomes (100% achieving  
 139 >6/12 vision), a significant 0% complication rate and a significantly reduced total cost to the  
 140 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		
<p><b>Abell &amp; Vote (2014)</b> Australia. Cost-effectiveness of Femtosecond Laser-Assisted Cataract Surgery versus Phacoemulsification Cataract Surgery</p> <p><b>Partially applicable</b> <sup>a</sup></p> <p><b>Potentially serious limitations</b> <sup>b,c,d,e</sup></p>	<p>Effects: Pragmatic literature review of cataract surgery outcome and complication rates.</p> <p>Costs: Australian Medicare Scheme schedule fees, AMA recommendations, private health insurance company annual reports, “current industry standards”. Patient payer costs included.</p> <p>Utilities: Based on a mathematical relationship with visual acuity</p>	<p>Costings are given without summary tables or justification of variability (unclear whether assumed costs). 3% discount rate used for costs only.</p>	928.61	0.01	\$92,861	<p>“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.”</p>	<p>Laser cataract surgery was considered most cost effective when 100% of patients achieved a BCVA of &gt;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.</p>

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



143

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

146 Pineda (2010) developed a decision-analytic model which examined the costs and outcomes  
147 among patients 65 years and older with cataract and pre-existing astigmatism (1.5–  
148 3.0 dioptres) who were allocated to either toric or conventional IOLs with and without  
149 intraoperative refractive correction (IRC). Data were obtained from a literature review of  
150 effectiveness studies, and a survey of ophthalmologists (n=60) conducted online in May  
151 2008. For each treatment option, ophthalmologists indicated the percentage of patients who  
152 would normally not need visual aids for distance vision following cataract treatment. They  
153 also indicated the percentage of these patients whose uncorrected visual acuity would be  
154 20/25 or better, worse than 20/25 to 20/40, and worse than 20/40 OU.

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

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

166 Patient utilities were based on data from a prospective study using the time trade-off and  
167 standard gamble methods among patients with various vitreoretinal diseases. Utility weights  
168 were calculated by converting the UCVA levels into Snellen decimal values (a midpoint was  
169 obtained for the level of 20/25 to 20/40 OU) and applying an equation derived by Brown et al.  
170 2000 ( $Utility = 0.37 \times UCVA + 0.514$ ). Each additional year after surgery was weighted by  
171 these utility values to derive quality-adjusted life years (QALYs), which were summed during  
172 18 years and annually discounted by 3% to compute cumulative lifetime estimates.

173 Disaggregated and total QALYs are not reported in the text. The base-case results suggest  
174 that incremental cost differences in treatment terms are small, and that over a lifetime  
175 horizon the use of toric IOLs generates a small saving in terms of patient- and provider-borne  
176 costs. At a 77% higher toric IOL cost or at a lower spectacle independence rate (worse-case  
177 scenarios), the toric IOL became the more expensive option during the patient's lifetime. The  
178 toric IOL was not a cost-saving option across the patient's lifetime if the frequency of  
179 changing glasses was reduced to once every 3 years. The use of the toric IOL compared  
180 with the conventional IOL without IRC resulted in cost savings as long as the remaining  
181 postsurgical lifetime was at least 16½ years (for all patients) or 17 years (for patients with  
182 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><b>Pineda et al. (2010)</b> 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><b>Partially applicable</b> a</p> <p><b>Very serious limitations</b> 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

185

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

190 **Malvankar-Mehta et al. (2013)**

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

203 **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

204

205 **Busbee et al. (2003)**

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

223 **Sach et al. (2010)**

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

226 successful cataract surgery and an operable cataract in the absence of other ocular  
 227 comorbidities. The comparison was patients on a watchful waiting list. HRQoL was measured  
 228 using the EQ-5D, and the payer perspective was NHS and PSS with carer costs included in  
 229 an additional scenario analysis. The mean total cost per patient for the lifetime analysis was  
 230 £12,171 and £10,887 in the operated and the control group, respectively. The incremental  
 231 cost-effectiveness ratio (ICER) for surgery in the base case was £17,299 per QALY gained.  
 232 The authors discuss the limitations of the EQ-5D for detecting both the quality of life of  
 233 patients with a cataract prior to surgery and the gain in HRQoL incurred through surgery,  
 234 highlighting this as a possible reason for their comparatively high ICERs relative to other  
 235 studies.

### 236 **Frampton et al. (2014)**

237 Frampton et al. (2014) developed a cost–utility model based on a systematic review of the  
 238 clinical effectiveness and cost effectiveness of second-eye cataract surgery. They identified 3  
 239 randomised controlled trials (RCTs) of clinical effectiveness, 3 studies of cost effectiveness  
 240 and 10 studies of health-related quality of life which met their inclusion criteria and, where  
 241 possible, were used to inform their economic analysis. Studies did not provide evidence that  
 242 second-eye surgery significantly affected HRQoL, apart from an improvement in the mental  
 243 health component of HRQoL as measured by the HUI (Health Utility Index -3) in 1 RCT. The  
 244 health economic analysis was conducted from the NHS and PSS perspective. It simulated a  
 245 cohort of patients undergoing either second-eye surgery or continued as unilateral  
 246 pseudophakia cases. In the surgery arm, people underwent successful surgery or had an  
 247 intra-operative or late complication (endophthalmitis, retinal detachment, PCO, cystoid  
 248 macular oedema (CMO), lost-lens fragments; with risks for PCO and retinal detachment  
 249 modelled time-dependently on a lifetime and 3-year time horizon respectively). Utility losses  
 250 and costs for adverse events were applied for 1 year, with costs and QALYs discounted at  
 251 3.5% per annum. Second-eye surgery generated 0.68 incremental QALYs with an ICER of  
 252 £1,964. Model results were most sensitive to changes in the utility gain associated with  
 253 second-eye surgery, but the procedure remained well below conventional limits at  
 254 £5,734/QALY even when a utility gain of as low as 0.02 was modelled. The model was  
 255 otherwise robust to changes in parameter values. The probability that second-eye surgery is  
 256 cost-effective at willingness-to-pay thresholds of £10,000 and £20,000 was 100%.

257 **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

258

Table 7 Economic evidence tables RQs 24 &amp; 25

Study, Population, Comparators, Quality	Data Sources	Other Comments	Disaggregated			Conclusions	Uncertainty
			Cost	Effect (QALYs)	Cost per QALY		
<p><b>Busbee et.al 2003</b> “Cost-utility analysis of cataract surgery in the second eye”.</p> <p>722 US patients (72yrs) undergoing cataract extraction in the PORT study. Comparator: Unilateral surgery (non-incremental)</p> <p><b>Partially applicable<sup>a</sup></b></p> <p><b>Very serious limitations</b> <sup>b,c,d,e, f</sup></p>	<p><b>Effects:</b> Assumed that the second eye VA would be equal to that of the first-operated eye.</p> <p><b>Costs:</b> Direct surgical costs of second eye surgery (zero costs for first-eye). Retinal procedures, drug expenditure for medical &amp; post-operative management. Medicare 2001 outpatient fee-schedule.</p> <p><b>Utilities:</b> Based on a mathematical relationship with VA.</p> <p><b>3% discount rate.</b></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><b>Sach et.al 2010</b> 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 <b>Directly applicable</b>  <b>Potentially serious limitations</b> <sup>a,b,c</sup></p>	<p><b>Effects:</b> EQ-5D in trial. Assumed that the utility difference between operated and unoperated eyes remains constant until death <b>Costs:</b> contacts with health and social services, care home admissions, informal care, equipment, and home modifications. Patient diaries. Deterministic. <b>Utilities:</b> In trial. EQ-5D at baseline &amp; 6 months. Effect difference assumed constant over lifetime. 3.5% discount rate. For costs and utilities.</p>	<p>Used a WTP threshold of £30,000 QALY</p>	£646	0.015	<p>1-year time horizon: <b>44,263</b> (no carer costs) <b>58,667</b> (costs of carer time included)</p> <p>Lifetime horizon: <b>17,299</b> (no carer costs) &amp; <b>41,973</b> (carer costs included)</p>	<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”</p>	<p>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

Study, Population, Comparators, Quality	Data Sources	Other Comments	Incremental vs no second-eye surgery			Conclusions	Uncertainty
			Cost	Effect	ICER		
<p><b>Frampton et al. (2014)</b> Simulated UK cohort of adults with cataract eligible for second eye surgery vs a hypothetical no surgery arm.</p> <p><b>Directly applicable.</b></p> <p><b>Minor Limitations</b> (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 &amp; 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>

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.

b) Patients had good vision pre surgery which may not represent all patients eligible for second-eye surgery.

## 264 J.3 Original cost–utility model – methods

### 265 J.3.1 Decision problem

266 **Table 8: Research questions**

<b>RQ3</b>	What are the indicators for referral for cataract surgery
<b>RQ4</b>	What are the optimal clinical thresholds in terms of severity and impairment for referral for cataract surgery

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

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

301 **Table 9: PICO**

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



**Outcomes**

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

302 Two separate decision problems were explored:

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

### 307 J.3.2 Overview of the model

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

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

#### 338 J.3.2.1 Modelled populations and interventions

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

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

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

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

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

#### 368 J.3.2.2 Model structure – general

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

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

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

391

**Table 10: Modelled health states**

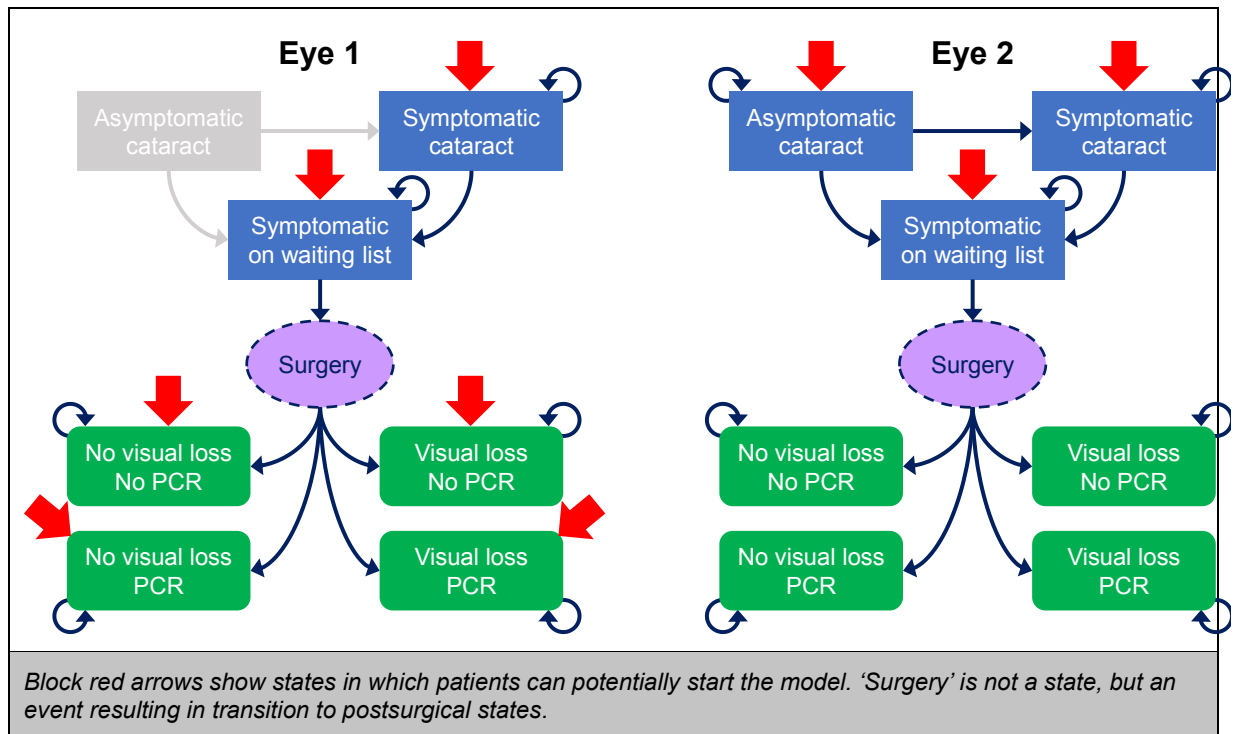
Health States	
Asymptomatic cataract	A state in which a cataract is present, but does not present symptomatically
Symptomatic cataract	A state in which a cataract is present and symptomatic, but the simulated patient is not currently listed for surgery. Patients remain in this state until death when '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

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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.

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396  
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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.



398

**Figure 1: Overall structure of original cost-utility model**

### 399 J.3.2.3 Model structure – first-eye surgery

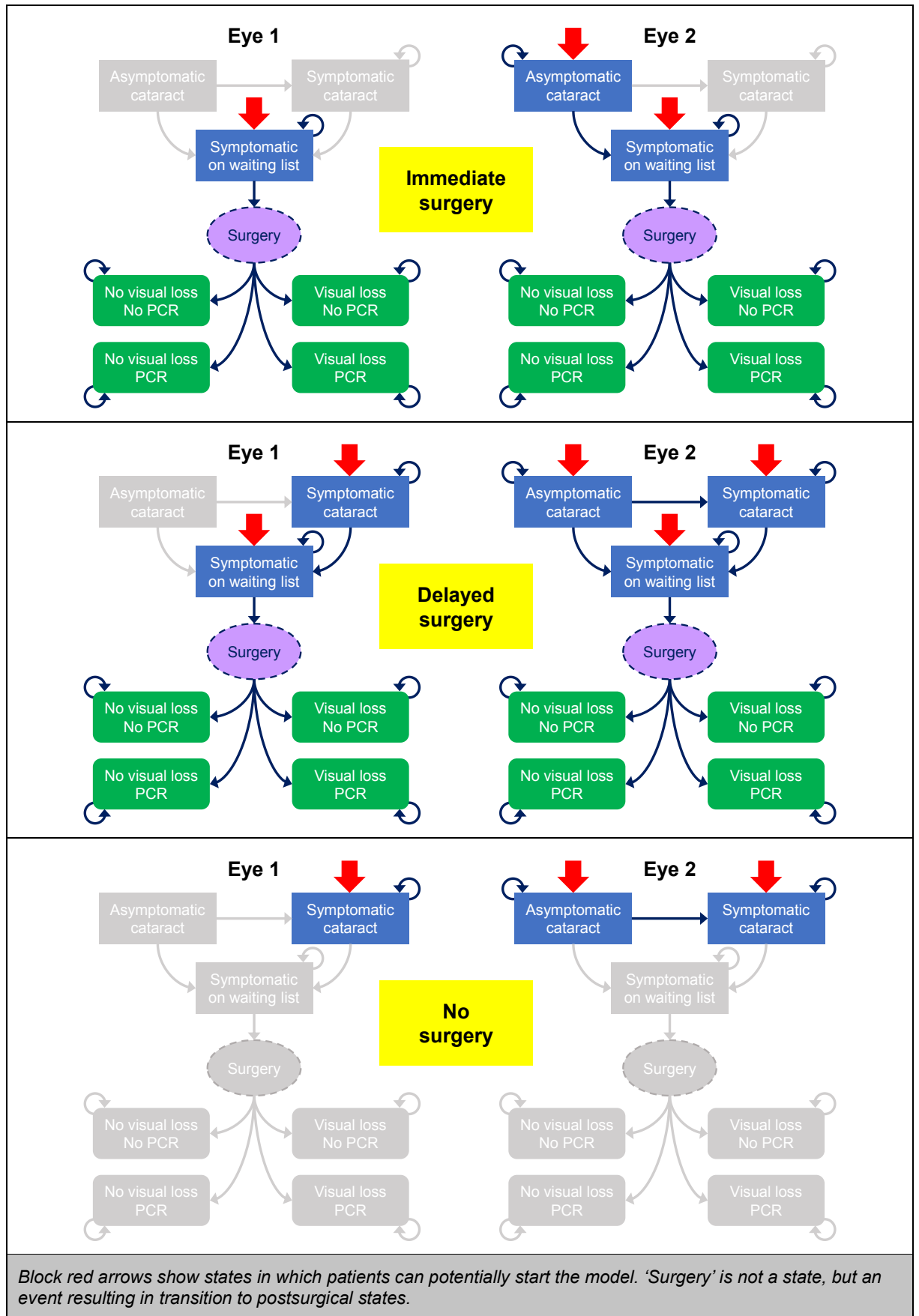
400 Figure 2 depicts how the general model structure is deployed in the 3 strategies simulated for  
401 the first-eye surgery decision problem.

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

### 418 J.3.2.4 Model structure – second-eye surgery

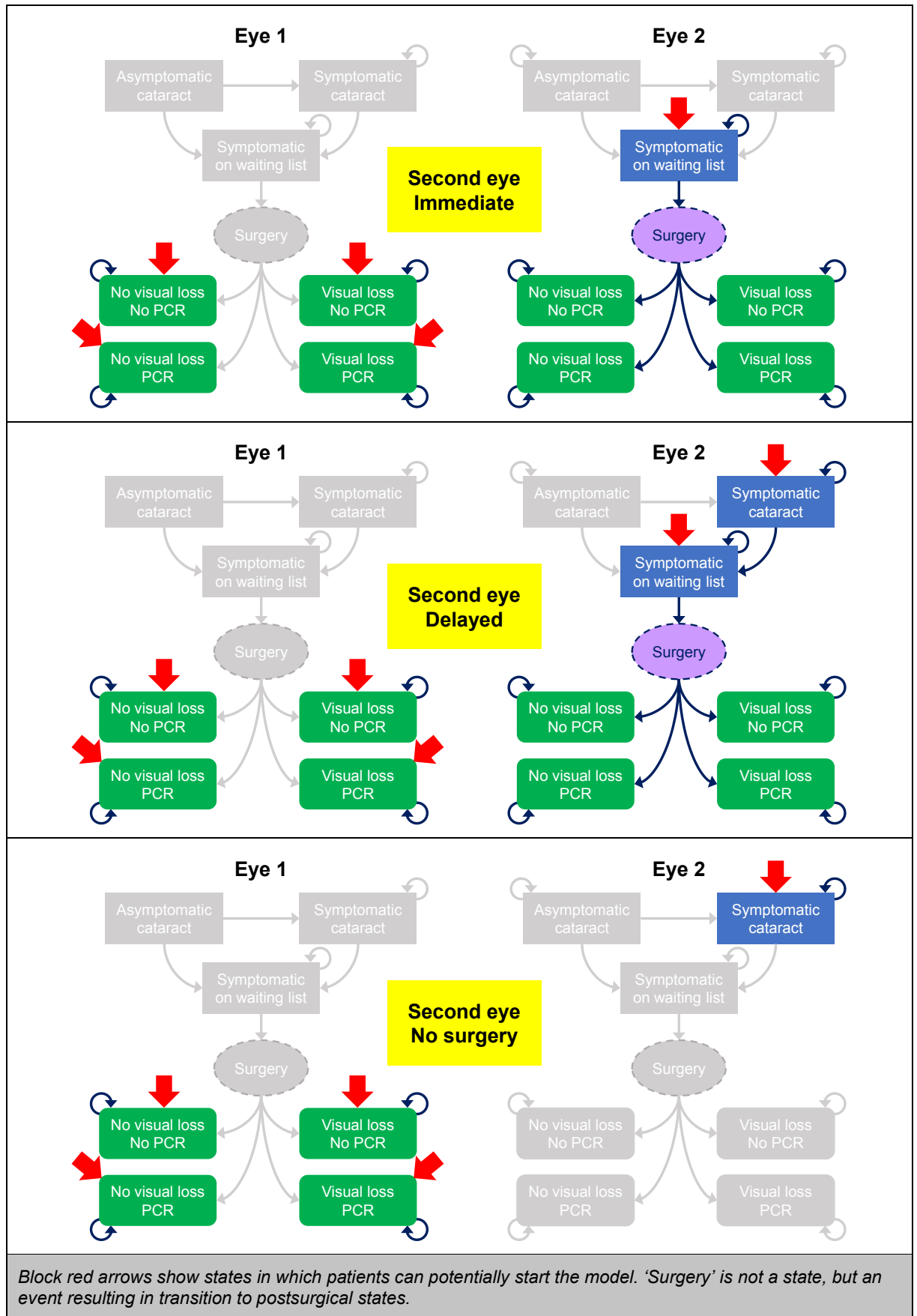
419 The model structure for second-eye surgery is similar, with some slight modifications. It is  
420 shown in Figure 3. Regardless of strategy, the first-eye in the second-eye surgery arm is  
421 assumed to be pseudophakic, that is – the first-eye has had a cataract successfully removed  
422 and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

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



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440

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



441  
442

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

443 **J.3.2.5 Key assumptions**

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

446 **Table 11: Key assumptions of original cost–utility model****Interventions**

- The model considers phacoemulsification cataract surgery only
  - 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.

**Natural history**

- 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

**Long-term effects**

- 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.

**Utilities**

- 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.

### 447 **J.3.3 Parameters**

#### 448 **Identifying sources of parameters**

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

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

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

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

#### 471 **Selecting parameters**

472 Our overriding selection criteria were as follows:

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

#### 482 **J.3.3.1 General**

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



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

### 492 J.3.3.2 Visual outcomes of cataract surgery

493 The RCOphth NOD provides data on baseline and postoperative visual acuity such that a  
 494 state-transition model could be built with individual states pertaining to Snellen/logMAR  
 495 ranges. However, this is impractical computationally as it increases the number of states  
 496 needed to incorporate memory into the model and provides little benefit to decision makers,  
 497 since costs and QALYs cannot be reliably attributed with available data to those VA state  
 498 transitions. Instead, we consider the dichotomous outcomes of “good” and “poor” visual  
 499 outcomes as defined by Sparrow et al. (2012) and Day et al. (2015) (where a poor outcome  
 500 is a doubling or worse of the visual angle, pre- to post-operatively – for example 6/12 – ≥  
 501 6/24).

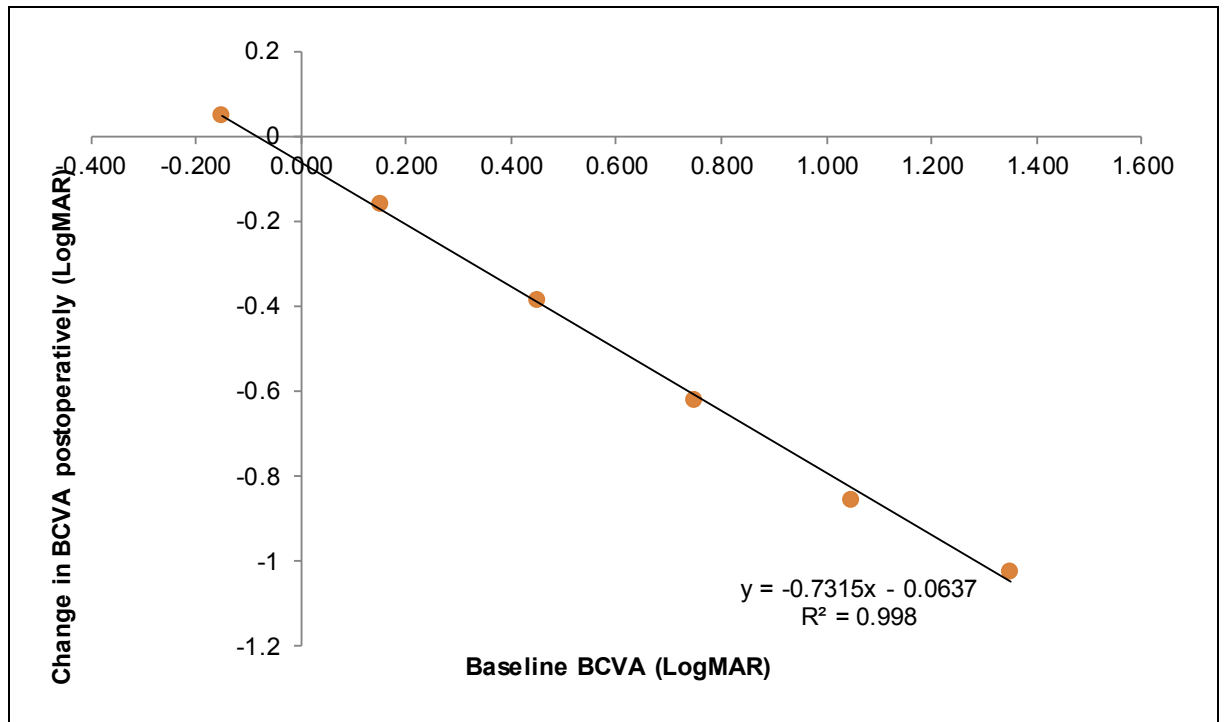
502 **Table 12 Matrix of baseline and post-operative visual acuity from Day et al. (2015)**

		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

503

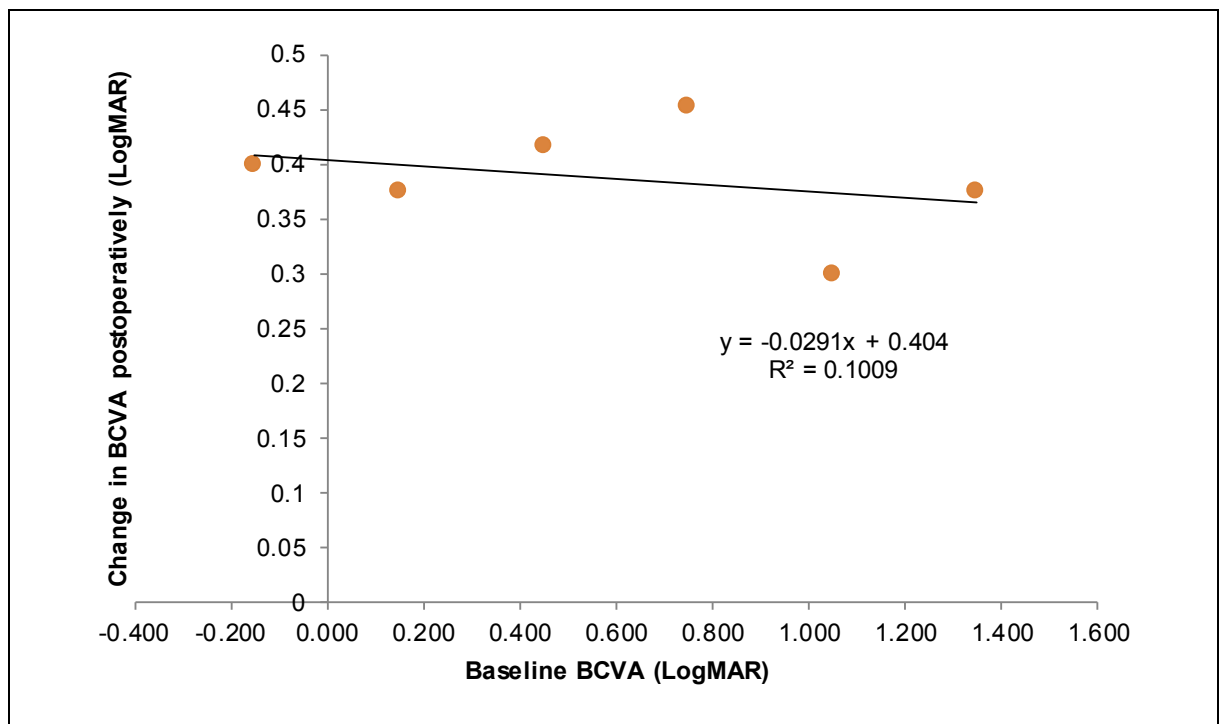
504 The outcome data (Table 12) published by Day et al. (2015) suggest that, regardless of  
 505 baseline VA, the modal postoperative visual acuity is 6/6 or better, which indicates that  
 506 cataract surgery results in good visual outcomes for the majority of cases. The data also  
 507 suggest an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

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



515  
516

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



517  
518

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

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

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

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

530 Multivariate models using the RCOphth NOD dataset have been published which can be  
531 used to calculate the probability of good or poor visual outcome based on patient and eye-  
532 related factors. Sparrow et al. (2012) constructed 3 multivariate models to examine the risk  
533 factors associated with VA outcomes in people undergoing cataract surgery. The authors  
534 developed a logistic regression model to assess candidate indicators for poor (doubling of  
535 visual angle or worse) visual outcome. The model incorporated data from 12 NHS trusts,  
536 totalling 406 surgeons across 55,567 cataract operations undertaken between 2001 and  
537 2006, for which post-operative VA outcomes were known for 40,758 (73.3%). All of the  
538 models adjusted for preoperative baseline VA as a continuous variable, and for inter-eye  
539 correlation by adjusting for paired eyes. The models incorporated the following covariates:

- 540 • age
- 541 • sex
- 542 • any ocular comorbidity
- 543 • age-related macular degeneration
- 544 • glaucoma
- 545 • diabetic retinopathy
- 546 • brunescient/white cataract
- 547 • high myopia
- 548 • corneal pathology
- 549 • amblyopia
- 550 • uveitis/synechiae
- 551 • no fundal view/vitreous opacities
- 552 • pseudoexfoliation/phacodonesis
- 553 • previous vitrectomy
- 554 • previous retinal detachment surgery
- 555 • axial length (quintiles)
- 556 • pupil size
- 557 • inability to co-operate
- 558 • unable to lie flat
- 559 • any alpha blocker
- 560 • tamsulosin, doxazosin, alfuzosin, indoramin, prazosin, terrazosin
- 561 • surgeon grade
- 562 • and PCR during surgery

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

568  
569**Table 13: Multiple logistic regression model of risk factors for poor visual outcome (cf Sparrow et al. 2012)**

Variable	Adjusted OR (95% CI)
<b>Age</b>	
<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)
<b>Axial length</b>	
≤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)
<b>Any ocular comorbidity</b>	
No	1.00
Yes	2.28 (1.87, 2.77)
<b>Diabetic retinopathy</b>	
No	1.00
Yes	1.73 (1.16, 2.59)
<b>Pupil size</b>	
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)
<b>Posterior capsular rupture</b>	
No	1.00
Yes	5.74 (3.93, 8.40)

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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.

580 **J.3.3.4 Posterior capsular rupture**581  
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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).

590  
591**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 $\geq 26.0$ 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)

592 **J.3.3.5 Progression of VA decline in people with cataracts**

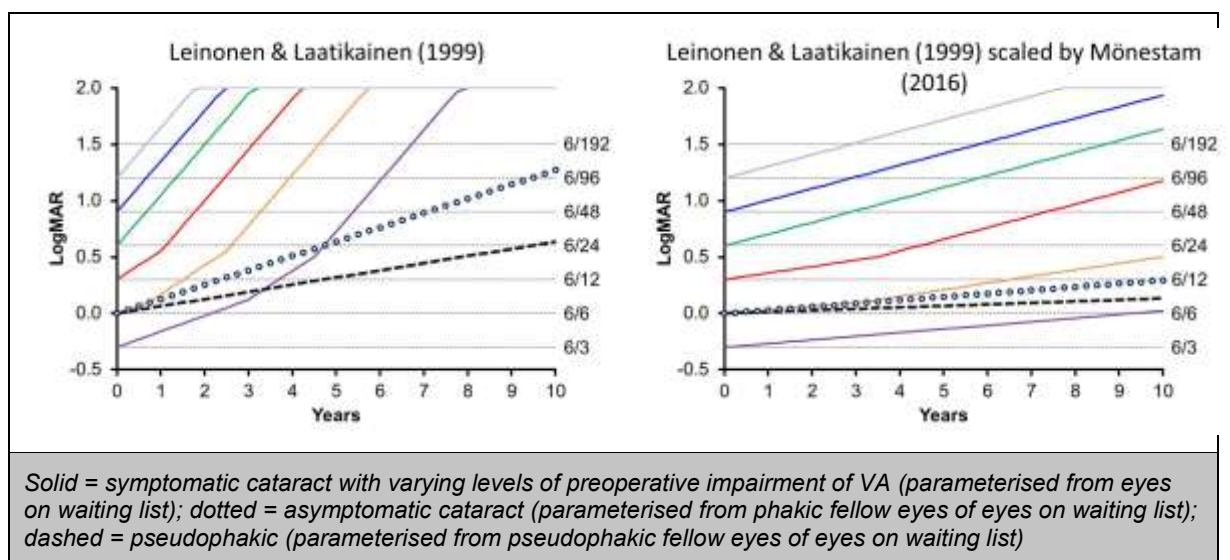
593 Given the considerable history of cataract surgery and broad evidence base for its  
594 effectiveness, surprisingly few studies of long-term follow up of patients post-cataract surgery  
595 have been published. Similarly, age-related visual changes are typically referenced to a  
596 limited number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

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

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

618 Mönestam (2016) conducted a prospective, longitudinal, population-based cohort study  
 619 detailing the visual acuity of patients at preoperative assessment, and at 5 yearly intervals  
 620 thereafter to 15 years post-surgery (Figure 5). The study included 190 patients (83% of  
 621 survivors). Fifteen years after surgery, the median CDVA in the operated eye had  
 622 deteriorated from 20/20 postoperatively to 20/25. Sixty percent of the patients had worsening  
 623 of CDVA of less than 0.1 logMAR units compared with postoperatively. These data provide  
 624 an indication of the visual decline observed over long-follow up in pseudophakic eyes.  
 625 Equivalent NHS data have not been published. We therefore use these data in our base  
 626 case to model the trajectory of visual acuity change in the post-operative period until death  
 627 as a constant linear decline. Leinonen and Laatikainen (1999) also publish data on the  
 628 pseudophakic fellow eyes (n=27) of people on the waiting list, which declined by 0.07  
 629 logMAR over the 13 month of follow up. This is a more rapid decline than in Mönestam  
 630 (2016) and, given the comparably short follow-up time of 13 months may reflect secondary  
 631 cataract (PCO) rates.

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

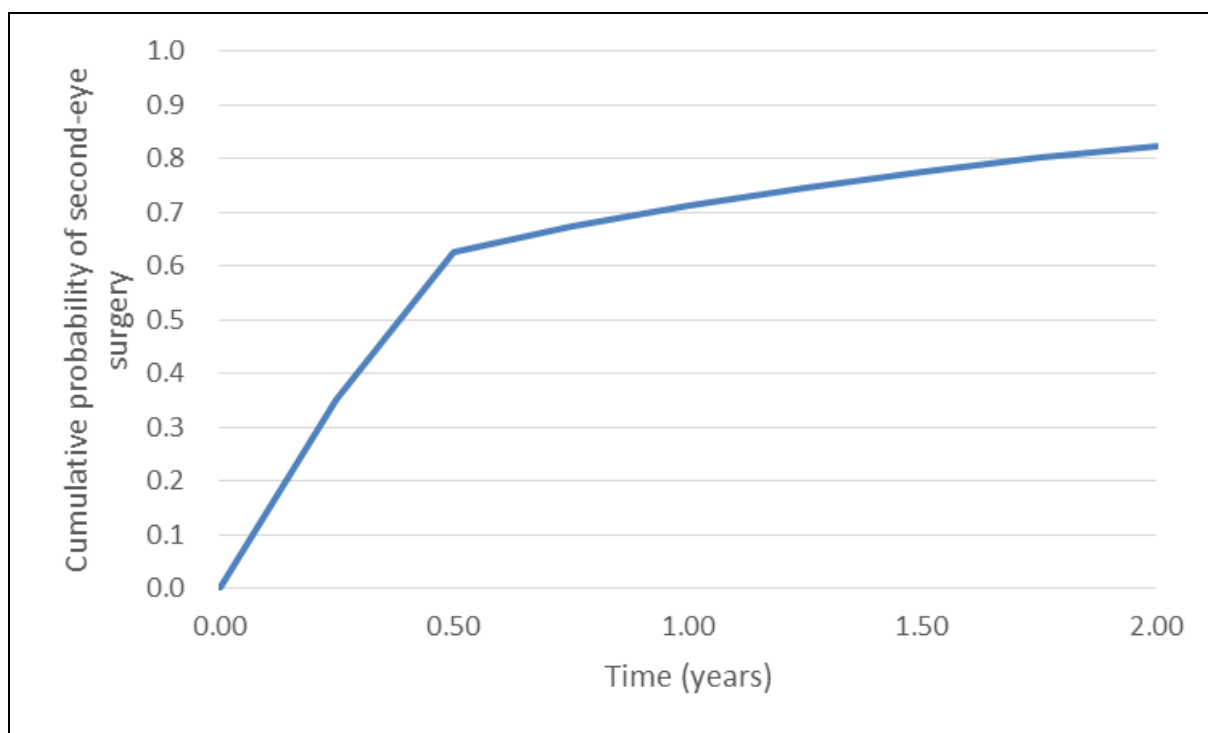


642 **Figure 6: VA changes over time in eyes before and after cataract surgery**

### 643 J.3.3.6 Simulating bilateral symptomatic cataract

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

646 as defined by their bilateral cataract would indicate referral for bilateral surgery, is 60%. This  
 647 is based on the RNIB campaign report from 2016, which reports that the maximum  
 648 proportion of second eyes that were operated on within 1 year of first-eye surgery was 60%.  
 649 We combine this with a study by Gollogly et al. (2013) who examined incident cataract  
 650 surgeries in Olmsted County, Minnesota, between 2005 and 2011 and described the  
 651 probability of second-eye cataract surgery using the Kaplan–Meier method. This suggests a  
 652 short time-interval between first- and second-eye surgery in most cases, with ~60% of  
 653 patients having the fellow-eye operated on three months after the index eye. We recognise  
 654 that in the US healthcare system waiting times will be shorter and capacity greater than in  
 655 the UK, but the data does provide a reasonable proxy measure (which agrees with the RNIB  
 656 estimates) for the proportion of people who have symptomatic contralateral cataract at the  
 657 initial referral. We use the slope of the Kaplan–Meier curve to calculate that an additional  
 658 10% of cases become symptomatic in the contralateral eye per annum after the peak at 60%  
 659 (see Figure 7). The probabilities of developing symptomatic cataract are detailed in Table 15.



660 **Figure 7: Cumulative probability of second-eye surgery**

661 **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

662

663 **J.3.3.7 Waiting list**

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

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

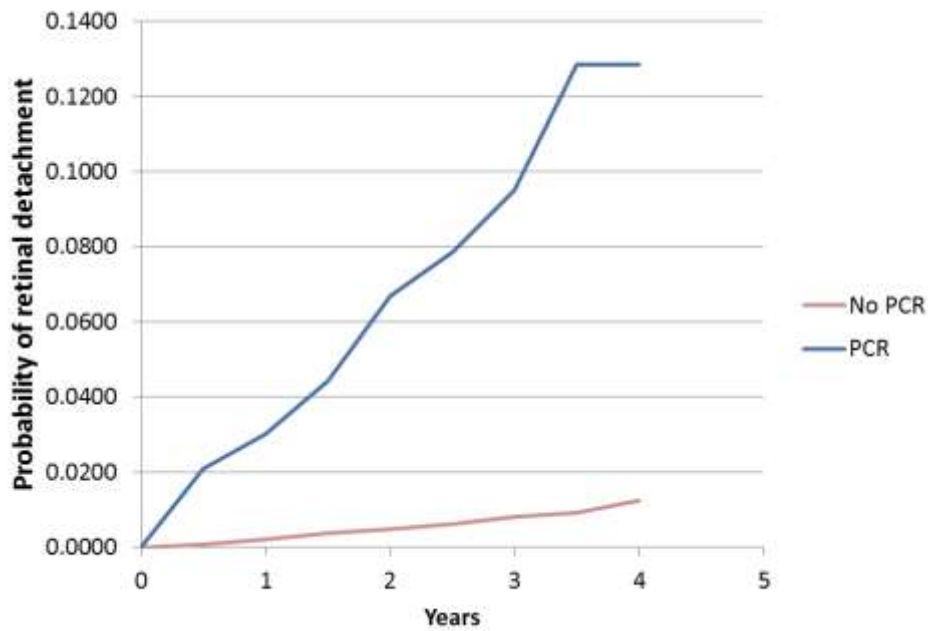
670 The waiting list state incorporates a variable time in state which is set at 129 days in the  
671 base-case analysis as per the mean waiting time for surgery in the RNIB audit (2016). A  
672 paper by Desai et al. (1999) suggests that waiting times for first and second eyes were  
673 similar at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

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

#### 687 **J.3.3.8 Retinal detachment**

688 Phacoemulsification surgery increases the risk of retinal detachment by moving the vitreous  
689 gel located behind the posterior capsule, which in turn can place traction and shearing force  
690 on the retina and lead to tears or punctures that precipitate detachment (Haug, 2012). Day et  
691 al. (2016) undertook a subgroup analysis of the RCOphth NOD from 13 sites where data on  
692 both cataract and vitreoretinal surgery were recorded on the same electronic medical records  
693 system. The study included 61,907 cataract operations performed between October 2006  
694 and August 2010. Analyses were restricted to cases with at least 3 months of potential  
695 postoperative follow-up. Pseudophakic RD surgery was performed on 131 eyes of 129  
696 patients (0.21%; 95%CI 0.18%-0.25%). Of these, 36 were in eyes that had PCR during  
697 cataract surgery (3.27%; 95%CI, 2.37%-4.50%) and 95 were in eyes that did not have PCR  
698 (0.16%; 95%CI, 0.13%-0.19%). We used the lifetable published in Day et al. (2016) to  
699 produce Kaplan–Meier plots of time to Retinal Detachment following cataract surgery in eyes  
700 with and without PCR (Figure 8). The data support the assumption that the rate of retinal  
701 detachment over a 4 year period follows an approximately constant rate and can therefore be  
702 parameterised as a constant probability following surgery.





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

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**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

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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.

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### J.3.3.9 Endophthalmitis

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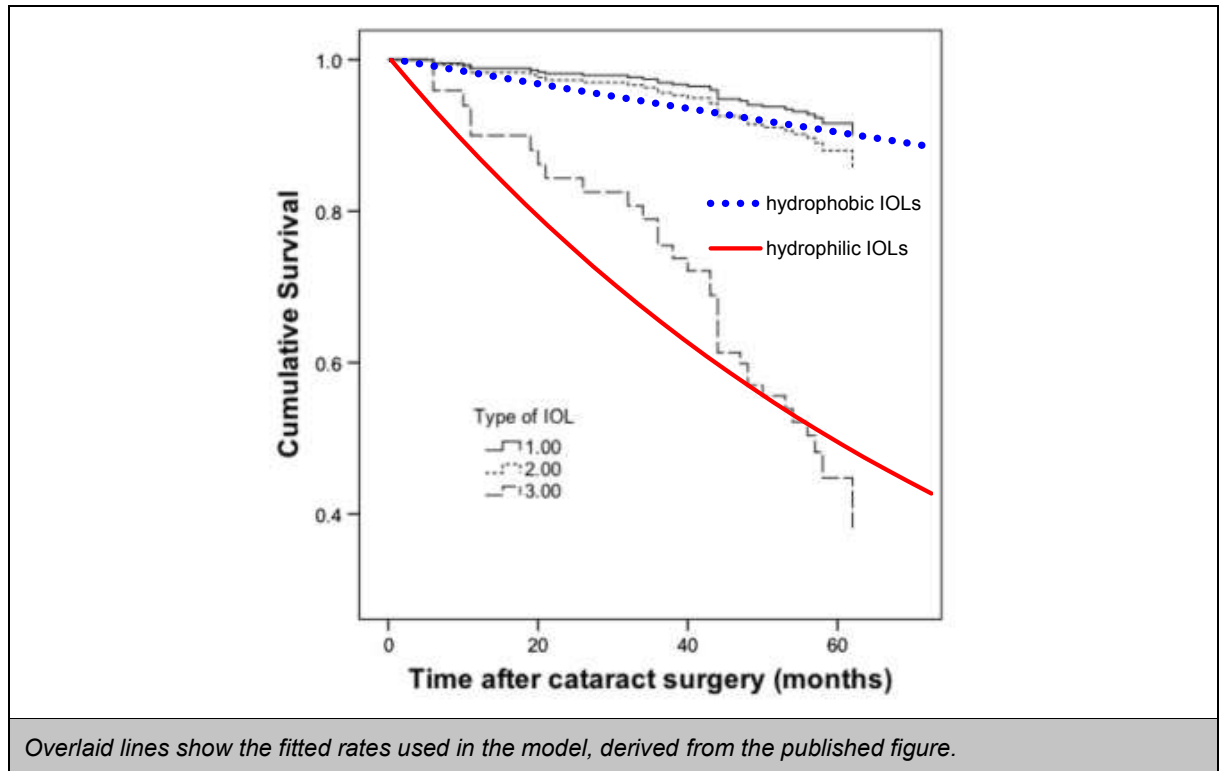
Endophthalmitis is an inflammation of the internal layers or 'coats' of the eye which is typically infectious in origin. It can cause poor visual outcome, and usually requires biopsy, antibiotics, and in some cases an emergency vitrectomy. Although endophthalmitis is a

717 relatively rare side-effect of cataract surgery, it incurs additional costs and can have long-  
718 term consequences for HRQoL when visual acuity is affected. Based on analysis of the  
719 RCOphth NOD, Day et al. (2015) presented data from 19 centres on 145,868 cataract  
720 operations (81% of the total number of surgeries in the database) for which postoperative  
721 (within 3 months of cataract removal) incidence data on endophthalmitis were available. The  
722 rate of endophthalmitis within 3 months of cataract surgery was 0.03% (43/145,868 cases,  
723 95% CI:0.02–0.04%). The rate of endophthalmitis was approximately 8 times higher (OR  
724 7.94, 95% CI: 3.35–18.83) in cases with PCR than those without. This translates to 0.026%  
725 (2½ per 10,000 cases) without PCR and 0.21% (21 per 10,000 cases) with PCR. We used  
726 these rates to calculate the probability of endophthalmitis in cases of surgery with and  
727 without PCR in the model.

#### 728 J.3.3.10 Posterior capsule opacification

729 Posterior capsule opacification (PCO) is a plaque which results from the growth and  
730 abnormal proliferation of lens epithelial cells which migrate to the posterior capsule. When  
731 the plaque approaches the central visual axis it causes visual-axis obscuration, resulting in  
732 dimness and clouding of vision. Symptomatic PCO is treated by a Nd:YAG laser  
733 capsulotomy, which involves using a laser to make a small hole in the posterior capsule that  
734 allows light through to the back of the eye, restoring normal vision. Whilst this is a common  
735 procedure, Nd:YAG capsulotomies also require additional outpatient visits which means they  
736 increase the overall cost of cataract surgery and therefore should be accounted for in an  
737 economic analysis. The clinical review for RQs 18 and 19 led the committee to recommend  
738 the use of hydrophobic IOLs to minimise the incidence of PCO and we therefore used this  
739 evidence to parameterise PCO rates in the model. The study by Sundelin et al. (2014) used  
740 Nd:YAG capsulotomy rates as a surrogate for PCO rates, using surveys and telephone  
741 interviews from 270 cases with a median follow-up time of 57 months (range 50–64 months).  
742 The 3-year cumulative incidence of PCO was 5.2% and the cumulative 5-year incidence was  
743 11.9%, and a survival analysis of capsulotomy stratified by lens type suggests that it is  
744 reasonable to assume a constant rate of capsulotomies (and thus PCO) over time (Figure 7).  
745 We use this evidence to calculate the per-cycle probability of PCO.

746



747

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

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#### 750 J.3.3.11 Mortality

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

#### 761 J.3.3.12 Resource use and costs

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

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

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

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

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

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

#### 780 J.3.3.13 **Costs of phacoemulsification cataract surgery with IOL implantation**

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

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

<b>Phacoemulsification cataract surgery: codes –</b> <b>BZ84A – CC Score 4+</b> <b>BZ84B – CC Score 2-3</b> <b>BZ84C – CC Score 0-1</b>	<b>N</b> <b>(used for</b> <b>weighting)</b>	<b>Cost</b>	<b>Lower</b> <b>IQR</b>	<b>Upper</b> <b>IQR</b>
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
<b>Weighted average cost</b>		<b>£858</b>		
<b>Cost with no PCR or endophthalmitis</b>		<b>£849</b>		

#### 789 J.3.3.14 **Costs of posterior capsule opacification (PCO)**

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

795

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

<b>Lens capsulotomy codes- BZ04A – CC Score 1+ BZ04B – CC Score 0</b>	<b>N (used for weighting)</b>	<b>Cost</b>	<b>Lower IQR</b>	<b>Upper IQR</b>
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
<b>Weighted average cost of Nd:YAG</b>		<b>£147.76</b>		
<b>Inflated to 2014/15</b>		<b>£149.09</b>		
<b>Including 2 Outpatient Appointments</b>		<b>£371.09</b>		

797 **J.3.3.15 Costs of endophthalmitis**

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

802 **Table 19 Costs of endophthalmitis: vitreous tap**

<b>BZ87A Minor Vitreous Retinal Procedures</b>	<b>N (used for weighting)</b>	<b>Cost</b>	<b>Lower IQR</b>	<b>Upper IQR</b>
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
<b>Weighted average cost of vitreous tap</b>		<b>£680.23</b>		

803 Additional costs for endophthalmitis were taken from Kamalarajah et al. (2004). In this study  
804 cases were identified prospectively by active surveillance through the British  
805 Ophthalmological Surveillance Unit reporting card system, for the 12-month period October  
806 1999 to September 2000 inclusive. Questionnaire data were obtained from ophthalmologists  
807 throughout the UK at baseline and 6 months after diagnosis. Their data suggest that 18% of  
808 patients require vitrectomy, and 38% of vitrectomies are performed urgently. We calculated a  
809 weighted average cost of vitrectomy from NHS Reference Costs, and then applied the  
810 incidence rates of surgical revisions as per Kamalarajah et al. (2004)

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

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

812 **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

813 **J.3.3.16 Costs of Retinal Detachment**

814 Based on discussions with the committee we parameterised the average cost of retinal  
815 detachment as being described by a case mix of vitrectomies, 75% performed as a non-  
816 elective procedure, and 25% as an elective day case. This gives an average cost of  
817 £1,832.18.

818 **J.3.3.17 Costs of PCR**

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

833 **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
<b>Additional cost of PCR</b>	<b>£405.80</b>		
<b>Additional cost of PCR inflated to 2014/15</b>	<b>£442.81</b>		

834 J.3.3.18 **Costs of low vision**

835 Vision-related healthcare resources are included in the model, required when a patient's VA  
 836 reaches a threshold level of impairment. Previous CUAs in various areas of visual  
 837 impairment have almost exclusively used estimates of the uptake of different low-vision  
 838 resources collated by Meads et al. (2003), originally from various sources. This defines the  
 839 proportion of people who register as sight impaired (94.5%), the uptake of low-vision aids  
 840 (33%) and low-vision rehabilitation (11%), and the use of services to treat vision-related  
 841 depression (39%) and hip replacements due to falls (5%). It provides estimates of the use of  
 842 PSS resources, namely the use of community care by home care workers (6%) and entry  
 843 into residential care (30%). It also provides estimates of the use of some non-NHS/PSS  
 844 resources due to severe sight impairment: housing benefit and council tax benefit (45%),  
 845 social security (63%) and tax allowances (5%).

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

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

NHS/PSS costs	Cost	Uptake %
<b>NHS/PSS costs of blindness</b>		
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%
<b>Non-NHS/PSS costs of blindness</b>		
Housing and council tax benefit	£2,714.40	45%
Social security	£3,029.84	63%
Tax allowance	£502.35	5%

853 J.3.3.19 **Background costs**

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

865 The costs for this scenario analysis were derived as follows. In the economic evaluations by  
 866 Sach et al. (2007 & 2010), post-intervention overall service use was higher in the operated  
 867 (first- and second-eye surgery) groups in the year after randomisation, particularly in the first  
 868 3 months after surgery. Significant differences in A&E attendances, outpatient visits, nurse

869  
870

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.

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**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
<b>First Eye</b>		
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	
<b>Per-cycle secondary care costs -- surgery</b>	<b>£53.32</b>	
<b>Per-cycle secondary care costs -- no surgery</b>	<b>£43.87</b>	
<b>Per-cycle primary care costs -- surgery</b>	<b>£401.75</b>	
<b>Per-cycle primary care costs -- no surgery</b>	<b>£161.95</b>	
<b>Second Eye</b>		
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	
<b>Per-cycle secondary care costs -- surgery</b>	<b>£53.32</b>	
<b>Per-cycle secondary care costs -- no surgery</b>	<b>£43.87</b>	
<b>Per-cycle primary care costs -- surgery</b>	<b>£401.75</b>	
<b>Per-cycle primary care costs -- no surgery</b>	<b>£161.95</b>	



873

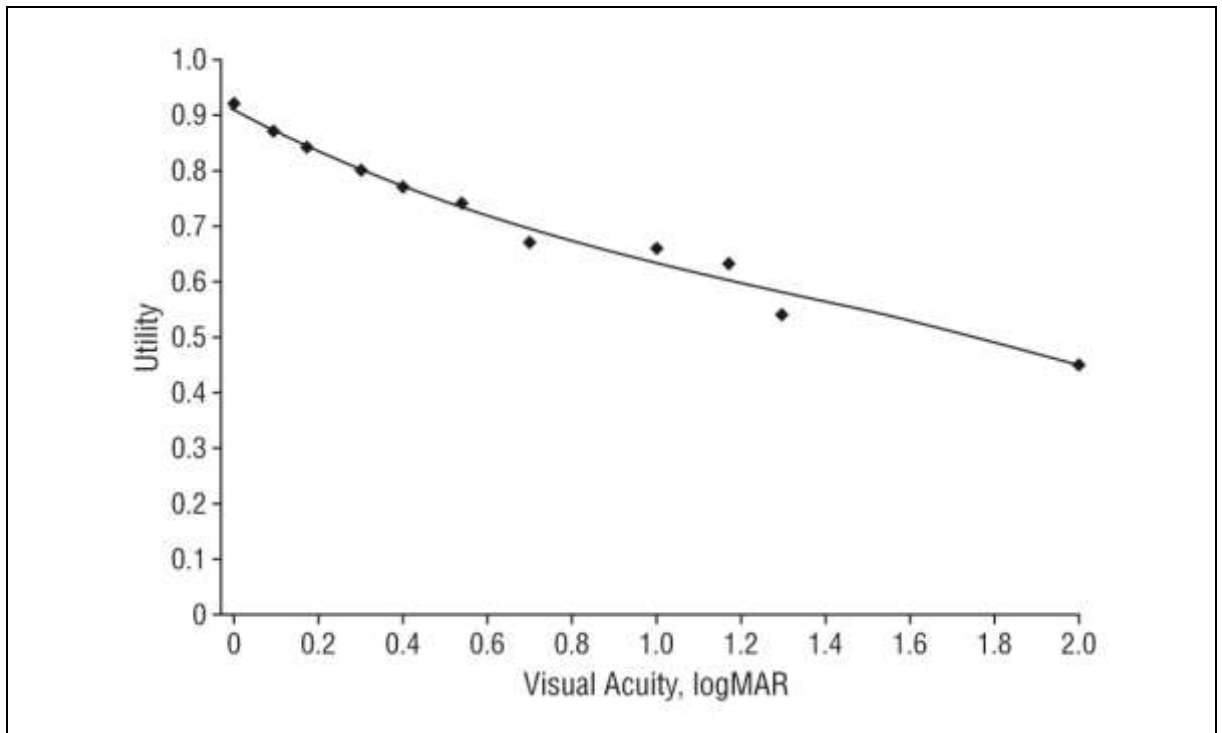
874 J.3.3.20 **Quality of life**

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

$$883 \text{TTO Utility} = -0.0479x^3 + 0.191x^2 - 0.4233x + 0.9128$$

884 where  $x$  is LogMAR acuity.

885 The model fit is shown in Figure 10.



886 **Figure 10: Third-order polynomial regression of VA on utility (from Lansingh et al.,**  
 887 **2009)**

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

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

899

900 **J.3.3.21 Adverse events**

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

907 **J.3.3.22 Retinal Detachment**

908 Rhegmatogenous retinal detachment is one of the most serious complications after  
 909 phacoemulsification combined with intraocular lens implantation surgery, with vision-related  
 910 quality of life (VRQoL), as well as visual acuity impacts that can be severe (Lina et al. 2016).  
 911 However, little is known of the VRQoL in those retinal detachment patients after anatomical  
 912 retinal re-attachment, especially whether or not the VRQoL is higher than that before cataract  
 913 surgery. In a prospective case series study, Zhu et al. (2015) assessed the changes of  
 914 VRQoL in age-related cataract patients who suffered from retinal detachment after  
 915 phacoemulsification with intraocular lens implantation. All participants were asked to  
 916 complete questionnaires in face- to-face interviews one day before and two weeks after  
 917 cataract surgery, as well as one day before and three months after retinal detachment  
 918 surgery. A total of 10,127 consecutive age-related cataract patients were followed up to  
 919 1 year after phaco-IOL implantation; among these patients, 17 were diagnosed with RRD.  
 920 The average utility differential reported in Zhu et al. (2015) is 0.82 (95%CI = 0.69-0.95) which  
 921 we applied as a multiplier to our modelled cohort in the cycle retinal detachment occurs but  
 922 assumed no further retinal detachment related HRQoL losses are experienced beyond that  
 923 point based on the committee's advice that RD is typically addressed within a 3-month  
 924 period.

925 **J.3.3.23 Endophthalmitis**

926 Clarke et al. (2008) compared quality of life in Australian patients who developed  
 927 endophthalmitis (19 cases) after cataract surgery between 1 January and 31 December 2003  
 928 with those who had uncomplicated surgery (31 controls). This study was retrospective  
 929 (1 year post-surgery) and so therefore evaluates the chronic rather than acute HRQoL  
 930 impact of endophthalmitis. The longer-term complications will be reflective of changes in  
 931 visual outcome and therefore these values are of most interest given the structure of our  
 932 model, although we acknowledge that this overlooks the acute effects of endophthalmitis,  
 933 which may not be negligible. We assume that endophthalmitis incurs a QALY loss in the year  
 934 in which it occurs, and that QALY decrement is then carried forward for the remaining life  
 935 expectancy on the assumption that the chronic symptomatic consequences of  
 936 endophthalmitis do not resolve.

937 **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		

938

**939 J.3.3.24 Other HRQoL Issues**

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

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

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

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

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

991 altogether, and instead postulate that utilities generated from direct elicitation methods using,  
992 for example, TTO, can be mathematically related to visual acuity scores. Thus, a patient with  
993 a visual acuity of a given LogMAR value can be assigned a utility score from which a QALY  
994 value can be inferred. The ability to extract QALYs (which are comparable across health  
995 domains) is a benefit of generic HRQoL instruments as it means that data from them can be  
996 used in cost–utility analyses. Data from disease-specific instruments can seldom be used for  
997 such analyses, typically because the instrument scores lack the societal preference based  
998 valuation needed to transform them into QALYs. For this reason, several authors have  
999 proposed mathematical techniques which map the scores from a disease specific index to a  
1000 generic tool such as the EQ-5D for the purposes of calculating QALYs. These mapping  
1001 algorithms constitute a fourth possible approach to incorporating HRQoL data from patients  
1002 with cataracts into economic models. This is a convenient methodology for extracting QALYs  
1003 when they would otherwise not be available, but it does not address the fundamental  
1004 problem that the index being mapped to may not be sensitive enough to capture changes in  
1005 HRQoL from cataract surgery.

1006 A 51-item Visual Function Questionnaire (VFQ) was developed in the United States using  
1007 focus groups of patients with a range of ocular pathologies and subsequently reduced to a  
1008 25-item survey based on an analysis of the 51-item responses (Cusick et al., 2005). The NEI  
1009 VFQ-25 has carer/physician administered and self-administered versions, and has been  
1010 validated and used to show that those with ocular disease and accompanying visual  
1011 impairment have lower scores compared with a reference group without ocular disease or  
1012 visual impairment . The use of self-report questionnaires to substitute for visual acuity  
1013 measurement has been limited, although the NEI-VFQ has been used in adult populations  
1014 (aged 40 years or more) to show that those with visual impairment have lower scores  
1015 compared with those without reduced visual acuity. However, concerns about the validity of  
1016 certain sub-scales used in the NEI-VFQ and its range of measurement have been raised  
1017 (Dougherty et al. 2010). In addition, use of the NEI VFQ in non-US populations is limited,  
1018 especially amongst older populations who are likely to experience higher levels of visual  
1019 difficulties than younger age groups.

1020 Rentz et al. (2014) address some of the problems of mapping to the EQ-5D (predominantly  
1021 the lack of sensitivity to visual acuity/visual function changes) by instead developing a  
1022 shortened form of the VFQ-25 (which is not limited by insensitivity to changes in vision) that  
1023 includes 6 domains: near vision, social vision; distance vision, role difficulty, vision  
1024 dependency and mental health. The 6 domains were selected by applying Rasch analysis to  
1025 the original VFQ-25 survey domains in order to eliminate problems of suboptimal  
1026 psychometric validity – which includes, for example, the ability for patients to provide  
1027 contradictory responses to multiple questions which are measuring similar properties. The  
1028 resulting index, VFQ-UI, was then tested on multiple cohorts with 8 vignettes presented to a  
1029 sample of the general population (n=607) in Australia, Canada, United Kingdom and the  
1030 United States. The results suggest that the index is capable of producing health states that  
1031 the general population consider as ranging across the continuum of perfect health to death.  
1032 However, there are abnormalities in the predicted utility values which may be a function of  
1033 the regression models used. The inclusion of age as a variable in the regression analysis is  
1034 opaque – it is unclear whether this refers to the age of the valuers or the age of a patient  
1035 described in the vignette. An additional anomaly is that the predicted utilities of patients  
1036 increases with age as a consequence of the age coefficient, when it would typically be  
1037 expected that healthy older patients would experience a baseline quality of life that is lower  
1038 (as a consequence of ageing) than younger people (Kind et al. 1999). The index is relatively  
1039 new, and thus far lacks validation and application in other studies. Further work is needed to  
1040 establish its sensitivity to changes in HRQoL associated with cataracts, including their natural  
1041 history and treatment.

1042 We discussed these various approaches with the guideline committee, and produced  
1043 example vignettes of how the VFQ-UI might reflect changes in HRQoL in patients with  
1044 cataract. The committee stated that more work, in the form of trial and validation studies,

1045 needed to be done in order for conclusions to be drawn on the best available method for  
 1046 measuring HRQoL in people with cataract. Establishing the impact of cataract and the benefit  
 1047 of cataract surgery in terms of QALYs gained remains an area of significant uncertainty.

### 1048 J.3.3.25 Summary of included parameters

1049 All parameters used in the model are summarised in Table 26, including details of the  
 1050 distributions and shape parameters. No probabilistic sensitivity analyses were undertaken for  
 1051 this work, so this table represents a library record.

1052 **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

### 1053 J.3.4 Presentation and interpretation of results

1054 The model includes 6 dimensions of data: baseline HRQoL, visual acuity in each eye, age,  
 1055 the probability of PCR, and the probability of visual loss. The possible combinations of these  
 1056 values runs into the several million, and therefore it is both sensible from the point of view of  
 1057 developing results that are useful to making recommendations, and desirable from a  
 1058 computational workload perspective, to rationalise these data by categorisation.

1059 We developed cut-off points for these data by first designing a usable matrix arrangement of  
 1060 variables, drawing from visualisation principals used by Leal et al. (2009) in their  
 1061 development of life-expectancy tables for people with type 2 diabetes. For HRQoL, we use  
 1062 natural breaks to characterise low, moderate and good categories as 0.4/ 0.6/ 0.8. We  
 1063 illustrate profiles for these natural breaks using the VFQ-UI. The VFQ-UI has 6 dimensions.  
 1064 The first three dimensions are questions about how eyesight affects activities of daily living  
 1065 and ask the following:

- 1066 1) How much difficulty do you have doing work or hobbies that require you to see well up  
 1067 close, such as cooking, sewing, fixing things around the house, or using hand tools? Would  
 1068 you say:
- 1069 2) Because of your eyesight, how much difficulty do you have seeing how people react to  
 1070 things you say?
- 1071 3) Because of your eyesight, how much difficulty do you have going out to see movies, plays,  
 1072 or sports events?

1073 These dimensions are graded as:

- 1074 1. No difficulty at all
- 1075 2. A little difficulty
- 1076 3. Moderate difficulty
- 1077 4. Extreme difficulty
- 1078 5. Stopped doing this because of your eyesight
- 1079 6. Stopped doing this for other reasons or not interested in doing this

1080 The fourth dimension of the VFQ-UI asks:

- 1081 4) Are you limited in how long you can work or do other activities because of your vision?

- 1082 This dimension is graded as:
- 1083 1. All of the time
- 1084 2. Most of the time
- 1085 3. Some of the time
- 1086 4. A little of the time
- 1087 5. None of the time
- 1088 The fifth and sixth dimensions of the VFQ-UI ask:
- 1089 5) I stay home most of the time because of my eyesight.
- 1090 6) I worry about doing things that will embarrass myself or others, because of my eyesight.
- 1091 These dimensions are graded as:
- 1092 1. Definitely True
- 1093 2. Mostly True
- 1094 3. Not Sure
- 1095 4. Mostly False
- 1096 5. Definitely False
- 1097 For HRQoL, we use natural breaks to characterise low, moderate and good categories as
- 1098 0.4/ 0.6/ 0.8. For illustrative purposes, a utility of 0.4 on the VFQ-UI would correspond to a
- 1099 health state of 323455 using the scoring methods described above, a utility of 0.4 would be
- 1100 described as health state 312445, and 0.8 as a health state of 211245. Exemplar VFQ-UI
- 1101 profiles are given in Subappendix Jc.
- 1102 For visual acuity, we use the 6 categories of logMAR acuity (as Snellen equivalents) given in
- 1103 Table 12, for both the index eye (the eye to be operated on) and the fellow eye. Age is
- 1104 simplified into 3 categories with midpoints of 60, 75 and 90 years.
- 1105 For the predicted probabilities of both PCR and visual loss, we used an iterative approach.
- 1106 Referring to the risk factor models previously described, we developed exemplar profiles with
- 1107 the lowest (no risk factors) and highest possible (all risk factors) predictive probabilities of
- 1108 PCR and visual loss, and then observed the changes in probability between these extremes
- 1109 as risk factors are added or removed from the model. Because these covariates are on
- 1110 logistic scales, the absolute risks of PCR and visual loss in low-risk and moderate-risk
- 1111 categories are much lower than some possible values of absolute risk for those profiles with
- 1112 many risk factors included. This is reflected in the midpoints adopted for low / moderate /
- 1113 high probability of PCR and visual loss which are set at 0.02 / 0.06 / 0.15 for both.
- 1114 The cross-categorisation across 6 domains results in a matrix of 2,916 unique scenarios,
- 1115 each representing some combination of age, VA in the index eye, VA in the fellow eye,
- 1116 baseline HRQoL, risk of visual loss, and risk of PCR. It may be useful to imagine this matrix
- 1117 as generating a very large number of subgroup analyses, with the model calculating a
- 1118 categorical value of utility-gain for each of the cells in the matrix, which represent each
- 1119 possible combination of variables (the subgroups). The full matrices are published in
- 1120 Subappendix Jd, at the foot of this document.
- 1121 These matrices show, for each possible combination of characteristics, the magnitude of
- 1122 immediate utility gain one would have to achieve in order to make surgery cost effective
- 1123 compared with no surgery or delayed surgery.
- 1124 Each matrix has 2 axes. The x-axis running horizontal at the top of the matrix is divided into 3
- 1125 parts from left to right, corresponding to the baseline HRQoL categories of low, moderate
- 1126 and good (0.4 / 0.6 / 0.8). In the stratum below this, there are 3 further subdivisions
- 1127 according to the risk of PCR (low, moderate, high). Each category of PCR risk is then
- 1128 subdivided into categories of risk of visual loss (low, medium, high). The y-axis running up
- 1129 the left vertical side of the matrix has a top-level stratum of 3 age categories (60, 75, 90).



1130 These age categories are divided into 6 levels of visual acuity in the index eye (the eye to be  
 1131 operated) from 6/6 to 6/96, which are each subdivided into the same visual acuity categories  
 1132 for the fellow-eye. This means that each cell in the matrix represents the magnitude of  
 1133 HRQoL gain needed for surgery to be cost effective given a combination of categories of  
 1134 age, baseline HRQoL, VA in both eyes, risks of PCR and risk of visual loss.

1135 We categorise the magnitude of HRQoL gain into the following brackets:

- 1136 • None = surgery would be cost effective even if it conferred no immediate HRQoL  
 1137 gain
- 1138 • Very small = greater than 0.00 but no more than 0.03
- 1139 • Small = greater than 0.03 but no more than 0.06
- 1140 • Moderate = greater than 0.06 but no more than 0.10
- 1141 • Large = greater than 0.10

1142 The rationale by which these categories were arrived at is detailed in Subappendix Jb.

1143 These can be applied to any index. The recently developed VFQ-UI, which has a societal  
 1144 preference valuation like the EQ-5D meaning it can be used to generate QALYs in cost-  
 1145 utility analyses, is one option that addresses some of the challenges inherent in estimating  
 1146 the impact of visual impairment of HRQoL. Tables Jc.1–Jc.4 illustrate baseline and post-  
 1147 cataract surgery HRQoL scenarios corresponding to our categorisation of HRQoL scores  
 1148 (very small, small, moderate and large gains post-surgery) side-by-side using the VFQ-UI.

### 1149 **J.3.5 Sensitivity analyses**

1150 We undertook sensitivity analyses which changed some key parameters and costs in the  
 1151 model. Firstly, an analysis was run which included the background costs from Sach et al.  
 1152 (2010) as detailed in section J.3.3.19, with reference to first and second-eye surgery, the  
 1153 effect being to increase the overall cost of surgery. Secondly, the committee had discussed  
 1154 the different visual acuity thresholds proposed by some trusts as a means of rationing  
 1155 surgery. While a 6/12 threshold was common, in some trusts a 6/9 threshold had been  
 1156 proposed as an alternative so we undertook a sensitivity analysis to explore the impact of  
 1157 this lower threshold on the cost-effectiveness of immediate vs delayed surgery. Thirdly, we  
 1158 explored the importance of cataract progression, which in our model is simulated as the rate  
 1159 of logMAR decline in symptomatic eyes. In section J.3.3.5 we discuss the way in which VA  
 1160 decline is parameterised in the base-case analysis as a weighted function of two studies  
 1161 which represent extremes of rapid and slower decline. In the sensitivity analysis we use the  
 1162 unweighted (more rapid decline in VA) data from Leinonen and Laatikainen (1999) to explore  
 1163 the impact of a more rapid progression on the model results.

1164 We discuss in section J.3.3.13 how we derived the cost of phacoemulsification cataract  
 1165 surgery. We spoke to experts on NHS Reference Costs and HRG grouping who confirmed it  
 1166 was reasonable to assume that the NHS reference costs would adequately describe the  
 1167 different lenses, medications, anaesthetics and intraoperative adverse events (aside from  
 1168 those requiring additional surgery and outpatient care) featuring in cataract surgery. Whilst  
 1169 we understand that the reference cost will incorporate, as a weighted proportion, the cost of  
 1170 more complex cataract surgery cases such as those requiring general anaesthesia, we have  
 1171 undertaken an additional sensitivity analysis that inflates the cost of phacoemulsification to  
 1172 account for these more complex cases. Our justification for doing this is twofold. Firstly, the  
 1173 precise mathematics of how the reference cost is calculated remains opaque, particularly  
 1174 with regard to how more complex cases are accounted for. Secondly, we have developed a  
 1175 model which explicitly deviates from considering the average level of benefit and instead  
 1176 considers the amount of benefit needed in many subgroups of risk factors for surgery to be  
 1177 cost-effective. It is appropriate therefore to explore the likelihood that higher-risk patients will  
 1178 incur higher than average costs, and examine the consequences of these additional costs on  
 1179 the model results. To this end, and in the absence of direct evidence of precise costs beyond

1180 expert opinion, we include a sensitivity analysis which increases the costs of  
1181 phacoemulsification by £500.

### 1182 J.3.5.1 Probabilistic sensitivity analyses

1183 Because of the model structure, and the departures therein from typical cost-effectiveness  
1184 analyses as discussed in section A.2.3.1, we did not produce a full PSA. This is usually done  
1185 to compare deterministic base-case results with probabilistically derived mean ICERs, and  
1186 produce CEACs. However, in this case the model does not produce ICERs which can be  
1187 used to inform recommendations for the RQs. It may be possible to run a PSA to develop  
1188 confidence intervals around the utility values which populate the decision matrix, but those  
1189 values are reported in categories rather than as point estimates and it is not clear how such  
1190 an analysis would add value to how the model is used to answer the relevant review  
1191 questions.

## 1192 J.4 Original cost–utility model – base-case results

### 1193 J.4.1.1 Results

1194 We provide summary results for all 2,916 possible combinations of the categories described  
1195 in J.3.4 in Subappendix Jd.

1196 In summary, the majority of modelled profiles show that cataract surgery is cost effective  
1197 even if there is no HRQoL gain, because immediate surgery avoids future QALY losses and  
1198 costs incurred by leaving the cataract(s) to progress either until death (in the no surgery arm)  
1199 or until a specified threshold value of acuity is reached. Where a gain in HRQoL is required it  
1200 is in the majority of cases only a very small gain.

### 1201 J.4.2 First-eye surgery

#### 1202 J.4.2.1 Immediate surgery compared with no surgery

1203 The full matrix for immediate surgery compared with no surgery in the first eye is shown in  
1204 Figure 26 in Subappendix Jd.

1205 In an overwhelming majority of scenarios (>99%), cataract surgery is shown to be cost  
1206 effective **even if it confers no immediate HRQoL gain**. This is because immediate surgery  
1207 avoids future QALY losses and costs incurred by leaving the cataract(s) to progress until  
1208 death.

1209 There are only 6 exceptions to this rule, all of which involve people aged 90 who have no  
1210 impairment of BCVA (6/6 vision) in the eye for which surgery is contemplated. If such people  
1211 have **either** very good **or** very poor vision in their other eye, and they are at high risk of **both**  
1212 PCR and visual loss, they would only be candidates for cost-effective surgery if it confers an  
1213 improvement in their HRQoL that can be classified as at least 'very small' (that is, a utility  
1214 gain of 0.00 to 0.03).

#### 1215 J.4.2.2 Immediate surgery compared with delayed surgery (threshold 6/12)

1216 The analogous matrix for the comparison of surgery with delayed surgery in the first eye is  
1217 shown in Figure 27 in Subappendix Jd. A relatively similar pattern is shown: most people  
1218 (85% of scenarios) are predicted to benefit from immediate surgery even if it confers no  
1219 HRQoL gain and, in those cases where a gain of HRQoL is necessary to justify the slightly  
1220 higher cost of immediate surgery, this benefit only has to be of 'very small' (that is, a utility  
1221 gain of 0.00 to 0.03) magnitude. There are a greater proportion of scenarios in which this  
1222 kind of expectation is necessary:

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- 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.

### 1236 J.4.2.3 Examples

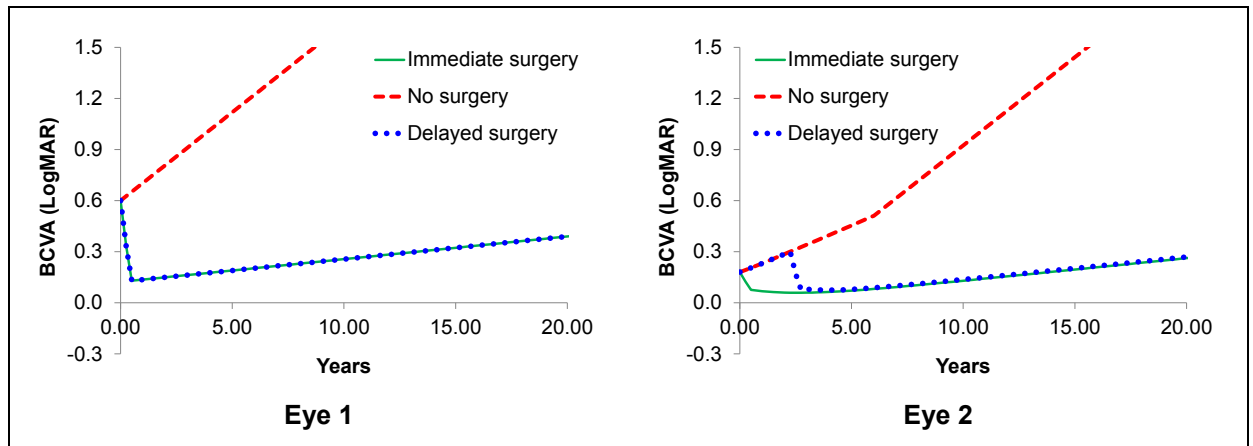
#### 1237 Example profile 1

1238 In this example, we consider the case specified in Table 27, which is a typical example of the  
 1239 large majority of cases in which no immediate HRQoL is necessary to make surgery cost  
 1240 effective – a 75-year-old with a low risk of PCR and poor visual outcome, with moderate  
 1241 impairment of best-corrected visual acuity in the worse-seeing eye and some impairment of  
 1242 BCVA in the fellow eye. In this case, the referral would be for first-eye surgery in a case  
 1243 where both eyes have some degree of cataract. The VA threshold in the delayed surgery  
 1244 arm is set to 6/12 in this example.

1245 **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)

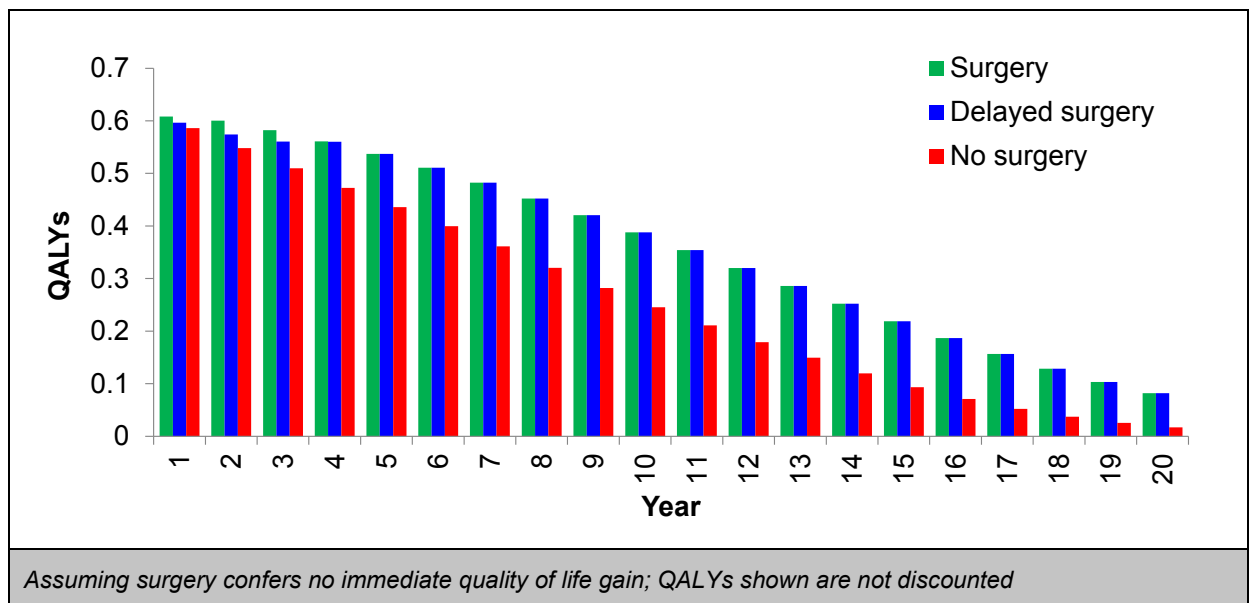
1246 Figure 11 details the modelled visual acuity trajectories of both eyes given immediate,  
 1247 delayed or no surgery. Because the first eye in this case is already past the 6/12 threshold or  
 1248 surgery the trajectories for the immediate and delayed surgical arms are identical for the first  
 1249 eye. In the no surgery arm visual acuity declines over time at the rate observed in Leinonen  
 1250 and Laatikainen (1999) scaled by the pseudophakic rate of VA decline in Mönestam (2016).  
 1251 For the second eye, the rate of decline in the no surgery arm and delayed surgery arm are  
 1252 identical, until the second eye has declined from 0.18 (6/9) to 0.3 (6/12) LogMAR, at which  
 1253 point surgery is simulated to take place, and the immediate and delayed surgery arms  
 1254 converge. The delayed strategy in this case incurs a loss of approximately 0.2 LogMAR  
 1255 before surgery, given the decline to 6/12 and then some further decline on the waiting list  
 1256 before surgery.



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

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1259 Figure 12 compares these strategies in terms of QALYs (before any immediate HRQoL gain  
1260 is applied to surgery). It can be seen that simply arresting the decline of acuity leads to  
1261 discernible QALY gains for immediate surgery. Note the convergence in immediate and  
1262 delayed surgery strategies after the VA threshold is met in the 3<sup>rd</sup> year. Beyond that point the  
1263 rate of VA decline, and therefore HRQoL decline, is identical for these strategies.



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

1264

1265 Table 28 shows the base-case incremental cost-effectiveness results for example profile 1,  
1266 and should be interpreted with the understanding that no immediate HRQoL benefit for  
1267 surgery is included (in other words, no QALYs are gained in this analysis, but the degree to  
1268 which they lost over time is modified by the timing of surgery, making this the most  
1269 conservative estimate possible of the cost effectiveness of surgery). The first thing to note is  
1270 that 'no surgery' is the most expensive option simulated. This is because, in this instance, the  
1271 costs of 'doing nothing' eventually substantially outweigh the costs of surgery, as the costs of  
1272 low-vision support accumulate, resulting from unchecked decline in acuity. Because 'no  
1273 surgery' is also associated with fewer QALYs than the surgical strategies, it is said to be  
1274 dominated and can be dismissed as a feasible option.

1275 The model estimates that performing immediate surgery costs an average of £112 more than  
1276 delaying it until a threshold of 6/12 is reached (in this case, this is solely a result of

1277 consequences for the second eye, as the first eye was already under the threshold at the  
 1278 time of presentation). This small saving comes from 2 places: the discounting effect of  
 1279 deferring costs for 3 or so years and the fact that a proportion of patients will die before they  
 1280 become eligible for second-eye surgery (whereas 96.6% of fellow eyes undergo eventual  
 1281 surgery in the 'immediate surgery' strategy, only 91.6% do if an acuity threshold is  
 1282 simulated). However, the extra money spent is predicted to confer a minimum of 0.057  
 1283 QALYs compared to delayed surgery. For an outlay of just over £100, a return of over 0.05  
 1284 QALYs would invariably be judged as extremely good value, with an ICER of £2,000 per  
 1285 QALY gained.

1286 **Table 28: Specimen base-case incremental cost-effectiveness results for example**  
 1287 **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*

## 1288 Example profile 2

1289 In this example we consider the case of an 80-year-old with a high risk of PCR and poor  
 1290 visual outcome, but with relatively good visual acuity in both eyes (see Table 29). In this  
 1291 case, the referral would be for first-eye surgery in a case where both eyes have some degree  
 1292 of cataract. The VA threshold in the delayed surgery arm is once more set to 6/12.

1293 **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)

1294 In this example (see Figure 13), the 'delayed surgery' and 'no surgery' arms track along the  
 1295 same trajectory until the threshold is reached for eye 1 and the transition to the waiting list  
 1296 and then surgery occurs. Because the VA in the second eye is better than eye 1, there is a  
 1297 longer period of decline along the no surgery trajectory in the delayed arm, reflecting the  
 1298 longer time taken for a cataract in a 6/6 eye to worsen to the VA threshold level.

1299 Note that, in both eyes, the immediate and delayed surgery arms do not quite converge,  
 1300 which reflects the somewhat increased risk of visual loss of performing surgery when the  
 1301 patient is older than at baseline.

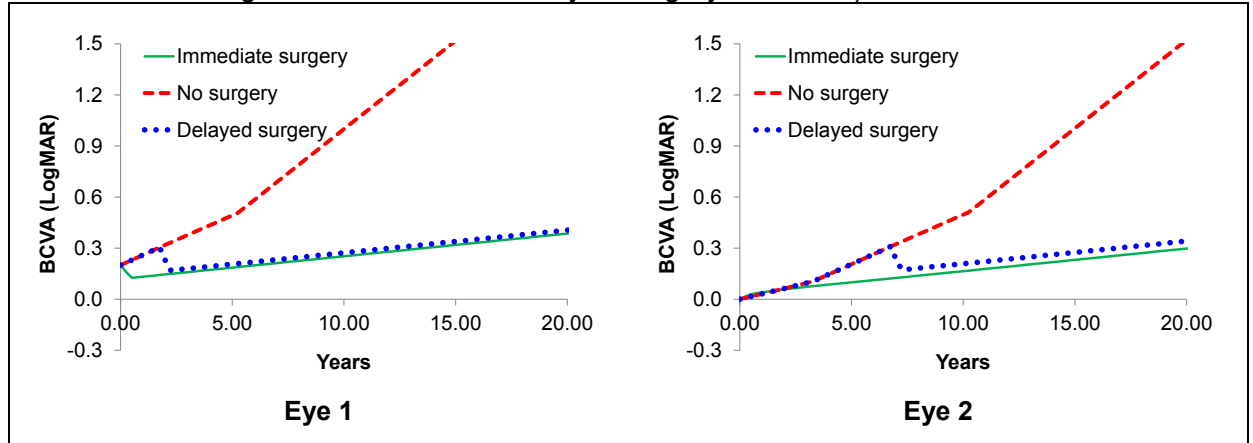
1302 Patients with a lower VA at surgery stand to gain, on average, more VA than those patients  
 1303 who undergo surgery with good visual acuity (see J.3.3.2, and Day et al. 2015).  
 1304 Consequently, the model predicts that our example patient undergoing immediate surgery in  
 1305 eye 2 ends up with BCVA that is very slightly worse, in the immediate postoperative period,

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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).

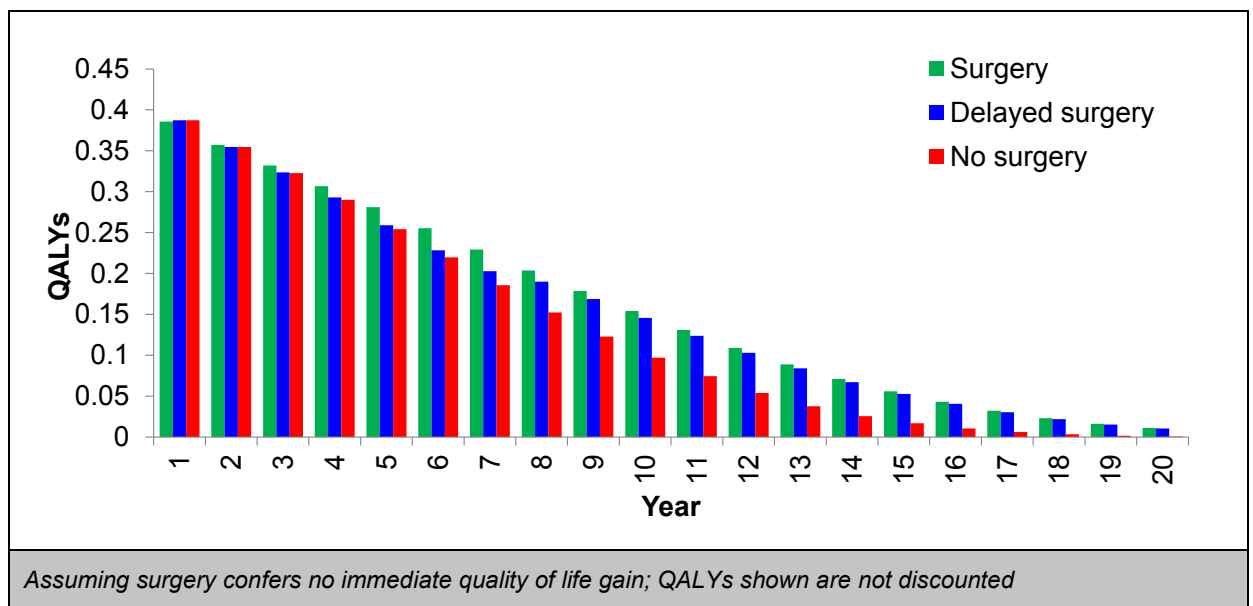
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Because of this, very slightly fewer QALYs are accrued in year 1 in the 'immediate surgery' arm than in the other arms. However, this initial small loss is offset as follow-up extends and the long-term benefit of early surgery accumulates (noting that,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



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



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

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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.

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**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*

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**Example profile 3**

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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.

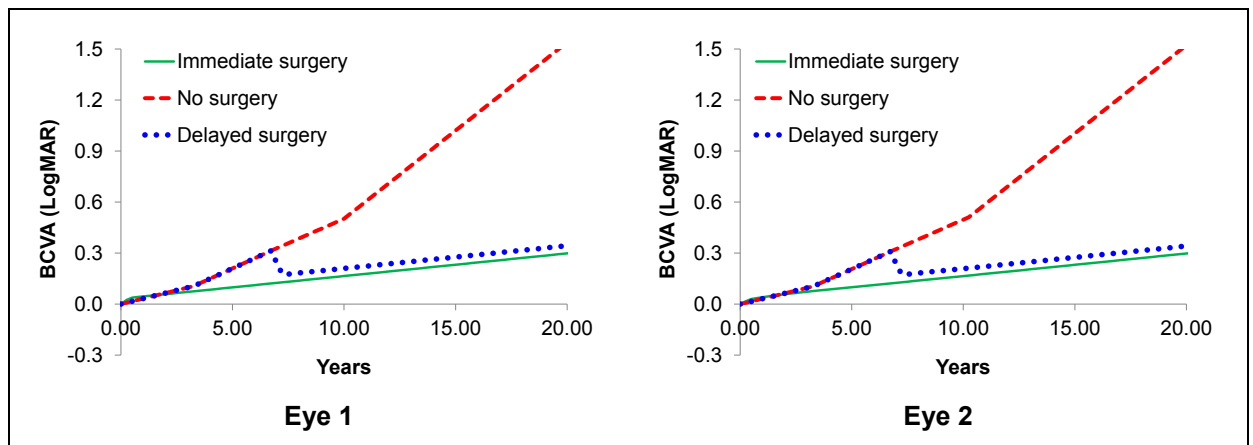
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**Table 31: Example profile 3**

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)

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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.

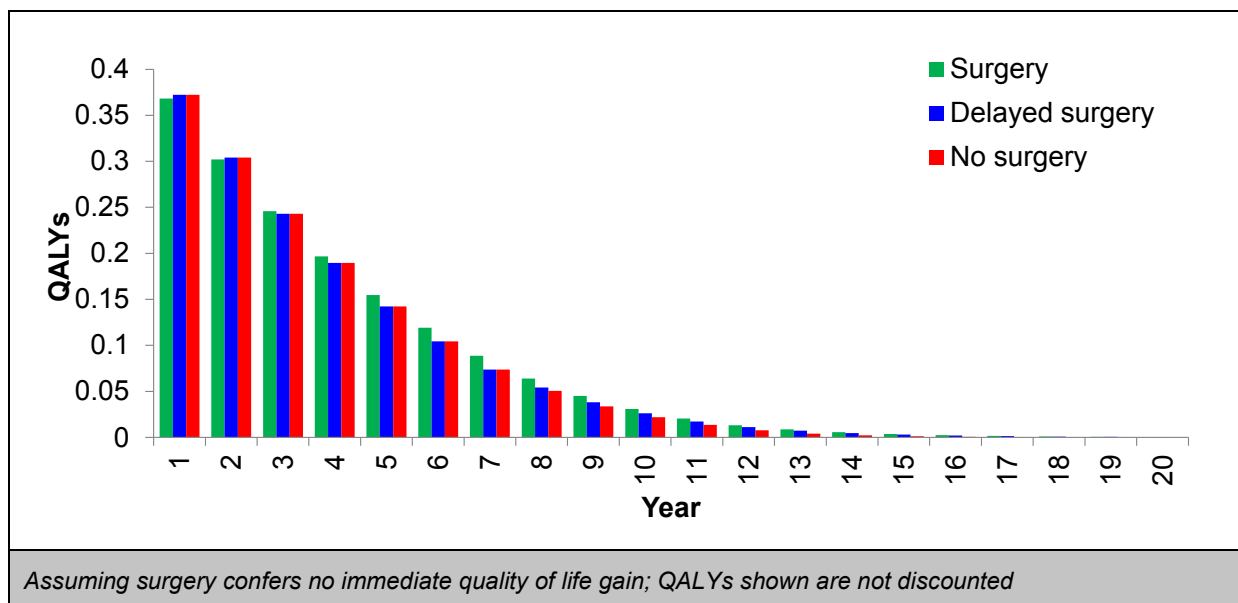


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**Figure 15: Visual acuity trajectories of both eyes for example profile 3 (base-case analysis)**

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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'.



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

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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.

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**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

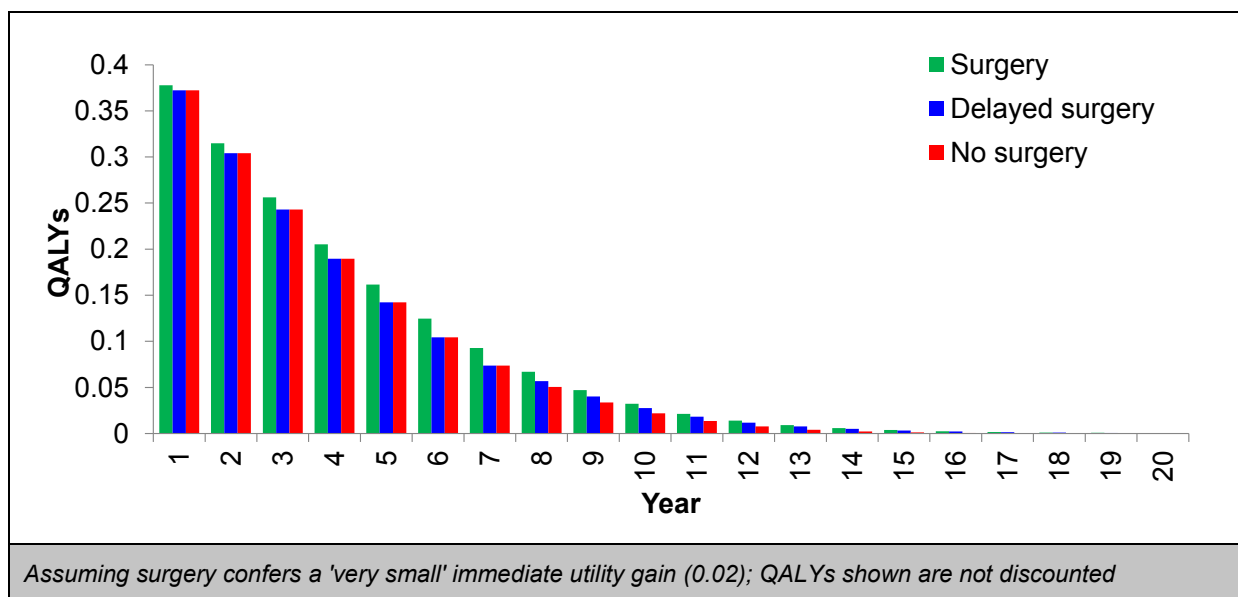
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However, as noted above, results for this profile change if we assume that surgery results in a 'very small' HRQoL gain (increasing utility by 0.02; see Subappendix Jc for an example of the kind of change in visual function that might be expected to 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



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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.



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**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)**

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**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)

1378 **J.4.2.4 Sensitivity analyses**

1379 **Faster rate of acuity decline**

1380 As explained in J.3.3.5, a rapid rate of acuity decline was observed in the Finnish waiting-list  
1381 study on which we base the trajectory of unoperated eyes (Leinonen and Laatikainen, 1999);  
1382 for this reason, in our base case, we scale these data by a factor that is derived from  
1383 analysis of another Scandinavian study (Mönestam 2016). However, in this sensitivity  
1384 analysis, we use the unscaled rate of decline.

1385 Results (no full matrix shown) suggest uniformly that no immediate improvement in HRQoL is  
1386 necessary to make surgery cost effective compared with no surgery or delayed surgery,  
1387 irrespective of the individual's characteristics and ocular risk factors. This is predictable: if we  
1388 believe unoperated eyes deteriorate at a rate of approximately 3 lines' BCVA per year (as

1389 suggested in the Finnish data), there is an urgent impetus to offer immediate surgery rather  
1390 than let people lose central vision in the eye in question.

### 1391 **Background NHS costs**

1392 When 'unrelated' costs are included (see J.3.3.19), cataract surgery becomes less cost  
1393 effective. Full results matrices are provided in Subappendix Jd.

1394 In the first version of this sensitivity analysis, these costs are assumed to apply in the first  
1395 postoperative year only (this is the period for which there are empirical resource-use data;  
1396 see J.3.3.19) and then revert to background level for subsequent years. Under this  
1397 circumstance, 'immediate surgery' is still associated with an ICER under £20,000 / QALY  
1398 compared with 'no surgery' in all scenarios featuring people under the age of 90, even when  
1399 surgery is assumed to confer no immediate benefit to HRQoL (Figure 30). For some of the  
1400 90-year-old profiles, an immediate HRQoL benefit of 'very small' magnitude is necessary to  
1401 make 'immediate surgery' cost effective and, in a very few cases where risk of both PCR and  
1402 visual loss is high and BCVA in the index eye is unimpaired, the benefit has to reach a  
1403 magnitude that could be classified as 'small' (see Subappendix Jc for illustrative examples of  
1404 changes in visual function that might meet these definitions). For the comparison of  
1405 'immediate surgery' and 'delayed surgery' (VA threshold 6/12; Figure 31), a small number of  
1406 scenarios in 60- and 75-year-old require a 'very small' immediate benefit to favour 'immediate  
1407 surgery'. Among 90-year-olds, most profiles require some degree of benefit and, in 3 cases  
1408 (all where the index eye has excellent BCVA, the fellow eye has very poor BCVA and the risk  
1409 of PCR and visual loss is high), 'immediate surgery' would not be cost effective compared  
1410 with 'delayed surgery' unless a 'medium'-sized benefit can be expected.

1411 In the second version of this sensitivity analysis, the additional, 'unrelated' costs are  
1412 assumed to apply in all postoperative years. This has a clear effect on the estimated cost  
1413 effectiveness of cataract surgery. As shown in Figure 32, 'immediate surgery' remains good  
1414 value for money compared with 'no surgery' for all 60-year-olds and most 75-year-olds.  
1415 However, when it comes to 90-year-olds, many cases would only be cost effective if an  
1416 HRQoL benefit can be assumed and, in some cases, that benefit would have to be 'large' to  
1417 outweigh the substantial additional lifetime costs that are now included. This requirement is  
1418 even clearer when 'no surgery' is compared with 'delayed surgery' (Figure 33).

1419 It should be emphasised that these sensitivity analyses represent a departure from the NICE  
1420 reference case, which states that such costs should be excluded. If it is to be believed that  
1421 receiving cataract surgery enables people to access healthcare resources for non-cataract  
1422 conditions they would otherwise not have consumed, it should also be hoped that the  
1423 additional healthcare is, in itself, cost effective and associated with benefits that cannot be  
1424 estimated in this model. Nevertheless, the sensitivity analysis is useful as to illuminate model  
1425 dynamics, which may remain opaque when almost all scenarios produce the same result.

### 1426 **Higher costs of cataract surgery**

1427 Raising the costs of cataract surgery has minimal effect on the model results for immediate  
1428 first-eye surgery compared with no surgery. A few additional cases in 90 year olds where  
1429 both the risk of visual loss and risk of PCR are high require a "very small" level of benefit in  
1430 order to be cost-effective, particularly when the index and fellow eyes have visual acuity of  
1431 6/12 or better. When comparing immediate surgery with delayed surgery, the additional costs  
1432 increase the number of cases in which a "very small" benefit is required in order for  
1433 immediate surgery to be cost-effective. This is evident in cases where the fellow eye is at 6/9  
1434 and the risk of PCR is low, moderate or high but not when the risk of visual loss is also high.  
1435 For people aged 90, the majority of cases require a benefit that is "very small" in order to  
1436 offset the additional costs, except for those cases where visual acuity in the fellow eye is 6/6  
1437 and the risk of both PCR and visual loss is high, wherein a "small" benefit is necessary for  
1438 immediate surgery to be the optimal strategy. For second eyes, the effect is similar to that

1439 observed in first-eyes but in all cases of 90 year olds at any level of risk when acuity is 6/6 in  
 1440 both eyes a “very small” benefit is required. This pattern is also observed in the comparison  
 1441 between immediate and delayed surgery for second eyes.

#### 1442 **Alternative – 6/9 – threshold for delayed surgery**

1443 A final sensitivity analysis explored the impact of a less stringent threshold for delayed  
 1444 surgery, LogMAR 0.18 (Snellen 6/9). A full results matrix for the first-eye decision-problem is  
 1445 shown in Figure 36 in Subappendix Jd. It shows that 'immediate surgery' is always estimated  
 1446 to be the optimal option in 60- and 75-year-olds. However, in the majority of scenarios  
 1447 among 90-year-olds, 'delayed surgery' represents a better balance of benefits and costs  
 1448 unless it can be assumed that surgery will make a difference to the patient's HRQoL that can  
 1449 be categorised as 'very small' or, when fellow-eye BCVA is severely impaired and risk of  
 1450 PCR and visual loss are both high, 'small' (see Subappendix Jc for illustrative examples of  
 1451 changes in visual function that might meet these definitions).

### 1452 **J.4.3 Second-eye surgery**

#### 1453 **J.4.3.1 Immediate surgery compared with no surgery**

1454 The full matrix for immediate surgery compared with no surgery in the second eye is shown  
 1455 in Figure 28 in Subappendix Jd.

1456 As for the first eye, cataract surgery is shown to be cost effective in most scenarios **even if it**  
 1457 **confers no immediate HRQoL gain**. This is because immediate surgery avoids future  
 1458 QALY losses and costs incurred by leaving the cataract(s) to progress until death.

1459 Compared with the first eye, there are slightly more scenarios in which HRQoL gain is  
 1460 necessary to produce an ICER lower than £20,000 / QALY; however, in common with the  
 1461 first eye, all these relate to people aged 90. In most cases, these scenarios also feature a  
 1462 high risk of visual loss. Whatever the other characteristics, an expectation of immediate  
 1463 HRQoL gain is needed when contemplating second-eye cataract surgery in a 90-year-old  
 1464 who has 6/6 vision in their fellow (pseudophakic) eye and a similar lack of impairment in their  
 1465 cataractous eye. Similarly, if risk of visual loss is high, immediate HRQoL gain is required for  
 1466 90-year-olds whose index eye is severely impaired (6/96) and whose pseudophakic eye is  
 1467 moderately severely impaired (BCVA 6/24–6/48), though this does not hold for people with  
 1468 6/96 impairment in both eyes (as they are subject to additional costs and mortality risk due to  
 1469 functional blindness, which can be relieved if surgery provides acuity gain in the index eye).

1470 In all these cases, only a 'very small' immediate HRQoL benefit is required to make surgery  
 1471 cost effective.

#### 1472 **J.4.3.2 Immediate surgery compared with delayed surgery (threshold 6/12)**

1473 The analogous matrix for the comparison of surgery with delayed surgery in the second eye  
 1474 is shown in Figure 29 in Subappendix Jd. A very similar pattern is shown: most people are  
 1475 predicted to benefit from immediate surgery even if it confers no HRQoL gain and, in those  
 1476 cases where a gain of HRQoL is necessary to justify the slightly higher cost of immediate  
 1477 surgery, this benefit only has to be of 'very small' magnitude. All these scenarios relate to 90-  
 1478 year-olds and most feature a high risk of visual loss.

#### 1479 **J.4.3.3 Examples**

##### 1480 **Example profile 4**

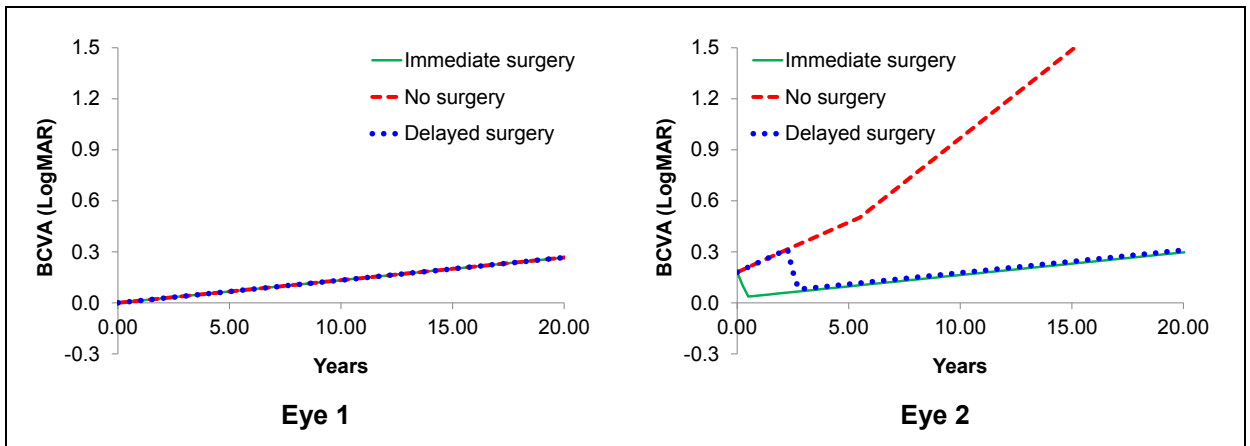
1481 In this example, we consider the case of a 75-year-old with a moderate of PCR and poor  
 1482 visual outcome, with visual acuity for both eyes as described in Table 34. In this case, the

1483 referral would be for second-eye surgery when first eye is pseudophakic (i.e has a history of  
 1484 cataract that has already been operated on, with an IOL implanted) and the second eye has  
 1485 an operable cataract. The VA threshold in the delayed surgery arm is set to 6/12 in this  
 1486 example.

1487 **Table 34: Example profile 4**

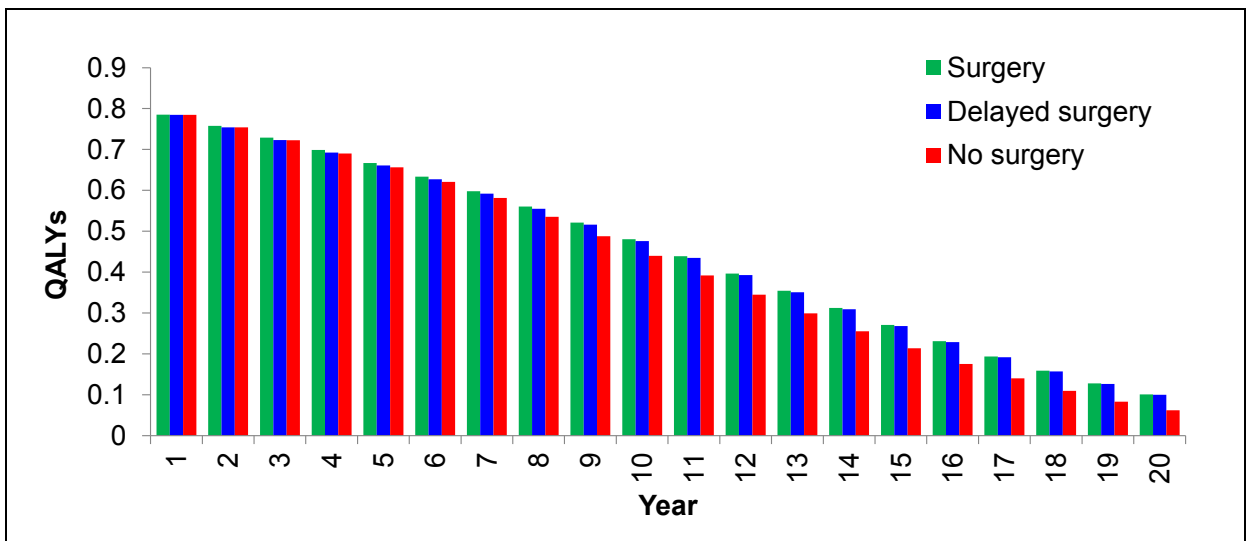
Variable	Value
Age	75
Starting BCVA (LogMAR), Eye1	0.00 (6/6)
Status of Eye1	Pseudophakic (second-eye surgery)
Starting BCVA (LogMAR), Eye2	0.18 (6/9)
Risk of PCR	0.06 (moderate)
Risk of poor visual outcome	0.06 (moderate)
Starting HRQoL	0.8 (good)

1488 In this profile (Figure 18), the pseudophakic first eye VA declines at a uniform rate while, as  
 1489 in previous examples, the VA in the 'delayed surgery' arm follows the 'no surgery' trajectory  
 1490 until 6/12 is reached and surgery occurs.



1491 **Figure 18: Visual acuity trajectories of both eyes for example profile 4 (base-case**  
 1492 **analysis)**

1493 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*

1494 **Figure 19: Annual QALYs for each strategy in example profile 4 (base-case analysis)**

1495 Incremental cost–utility results for this profile are shown in Table 35. In this example,  
1496 'delayed surgery' is extendedly dominated. Extended dominance rules out any intervention  
1497 that has an ICER that is greater than that of a more effective intervention. This is based on  
1498 the assumption that decision-makers, when seeking to maximise value for money, will prefer  
1499 the more effective intervention that has a lower incremental cost-effectiveness ratio thereby  
1500 purchasing QALYs in a more efficient manner.

1501 'Immediate surgery' is estimated to provide around 0.5 QALYs compared with 'no surgery', at  
1502 an additional cost a little under £2,000, leading to an ICER of under £4,000 / QALY. If QALYs  
1503 take NICE's usual valuation of £20,000 each, this would be seen as a strongly cost-effective  
1504 intervention.

1505 **Table 35: Specimen base-case incremental cost-effectiveness results for example**  
1506 **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*

1507 **Example profile 5**

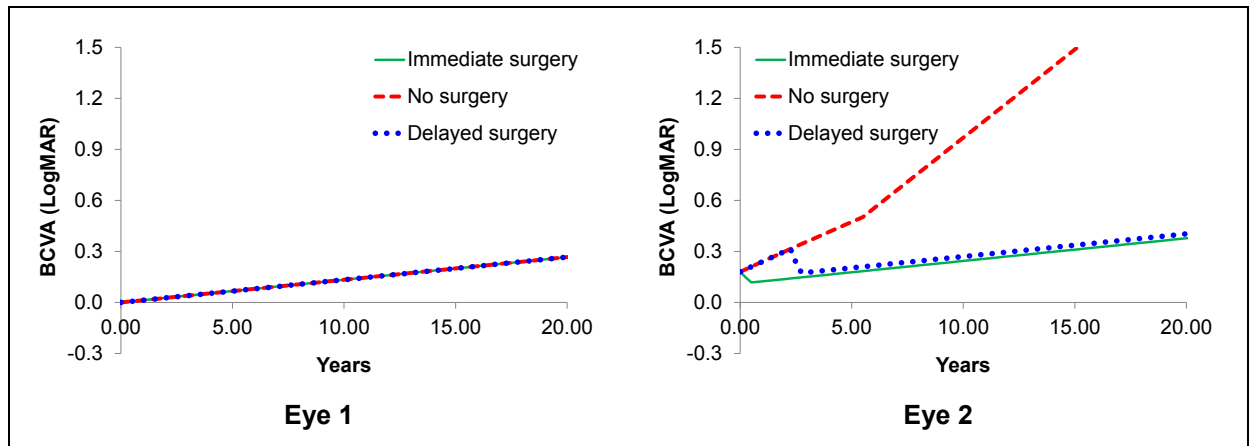
1508 In this example, we consider a case that requires some immediate HRQoL benefit to justify  
1509 second-eye surgery. The scenario – set out in Table 36 – is similar to example 4, except the  
1510 population is now aged 90 and the risk of PCR and visual loss has become high.

1511 **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)

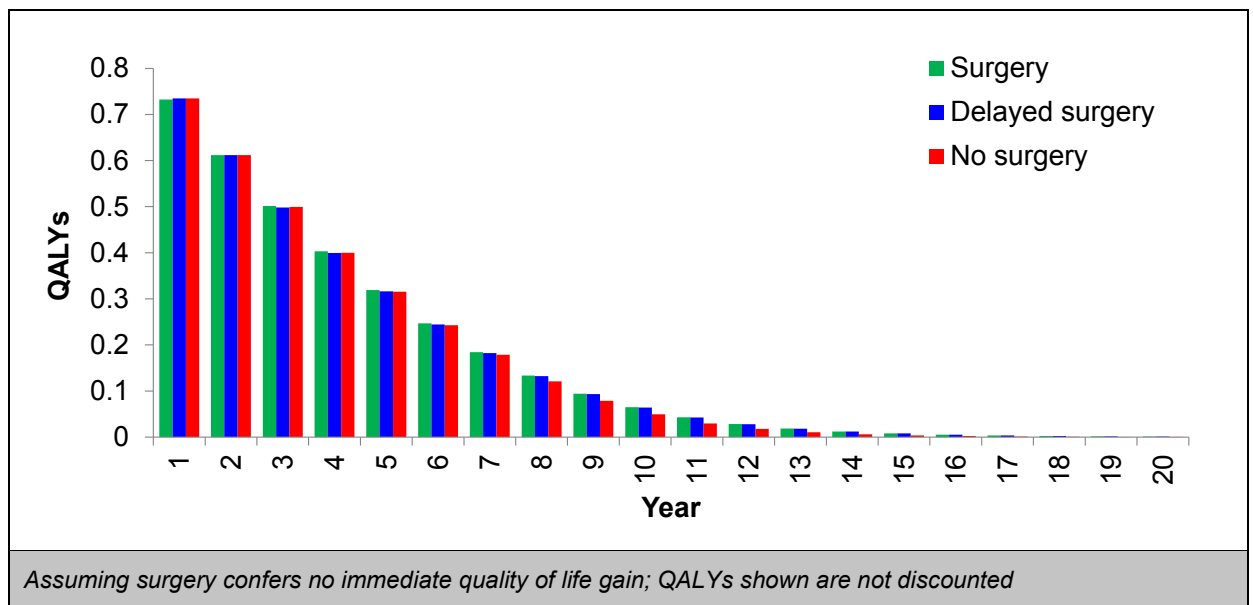
1512 In this profile (Figure 20), we again see uniform, gradual deterioration in the pseudophakic  
1513 first eye

1514 as in previous examples, the VA in the 'delayed surgery' arm follows the 'no surgery'  
1515 trajectory until 6/12 is reached and surgery occurs.



1516 **Figure 20: Visual acuity trajectories of both eyes for example profile 5 (base-case**  
 1517 **analysis)**

1518 Expected year-by-year QALYs are shown in Figure 21.



1519 **Figure 21: Annual QALYs for each strategy in example profile 5 (base-case analysis)**

1520 Incremental cost–utility results for this profile are shown in Table 37. In this case, the optimal  
 1521 strategy, assuming we do not want to pay more than £20,000 for additional QALYs, is  
 1522 'delayed surgery'. In comparison, only a small benefit (around 0.01 QALYs) is gained by  
 1523 performing surgery immediately, and the associated cost leads to an ICER of very nearly  
 1524 £30,000 / QALY.

1525 **Table 37: Specimen base-case incremental cost-effectiveness results for example**  
 1526 **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>					

1527 However, as noted above, results for this profile change if we assume that surgery results in  
 1528 a 'very small' HRQoL gain (increasing utility by 0.02; see Subappendix Jc for an example of  
 1529 the kind of change in visual function that might be expected to lead to this amount of benefit).  
 1530 Table 38 shows incremental cost–utility results with a HRQoL gain of 0.02 ascribed to  
 1531 surgery. Here, the incremental benefit of 'immediate surgery' over 'delayed surgery' rises to  
 1532 around 0.04 QALYs, with no change in incremental costs, leading to an ICER a little under  
 1533 £10,000 / QALY. Therefore, if we are content to assume that surgery improves people's  
 1534 quality of life by at least a 'very small' amount, 'immediate surgery' would become the  
 1535 preferred option.

1536 **Table 38: Specimen base-case incremental cost-effectiveness results for example**  
 1537 **profile 5, with a 'very small' immediate quality of life benefit ascribed to**  
 1538 **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>					

#### 1539 J.4.3.4 Sensitivity analyses

##### 1540 Faster rate of acuity decline

1541 As with the first eye, results (no full matrix shown) suggest uniformly that, if the BCVA of  
 1542 eyes with cataracts deteriorates at the speed observed by Leinonen and Laatikainen (1999),  
 1543 no immediate improvement in HRQoL is necessary to make surgery cost effective compared  
 1544 with no surgery or delayed surgery, irrespective of the individual's characteristics and ocular  
 1545 risk factors.

##### 1546 Background NHS costs

1547 The results for these sensitivity analyses are similar to those seen for the first eye (see  
 1548 J.4.2.4). Once more, when 'unrelated' costs are included (see J.3.3.19), cataract surgery  
 1549 becomes less cost effective. Full results matrices are provided in Subappendix Jd.

1550 If the 'unrelated' costs are applied to the first postoperative year only (Figure 37, Figure 38),  
 1551 results change for 90-year-olds only. Here, there are multiple scenarios in which an  
 1552 immediate HRQoL benefit of 'very small' magnitude is necessary to make 'immediate  
 1553 surgery' cost effective compared with 'no surgery' or 'delayed surgery', and a small number  
 1554 where a 'small' benefit has to be assumed to achieve the same result (always where BCVA  
 1555 in the cataractous eye is 6/6 and the risk of both PCR and visual loss is high. See  
 1556 Subappendix Jc for illustrative examples of changes in visual function that might meet these  
 1557 definitions.

1558 When the additional costs are assumed to apply in all postoperative years, some degree of  
 1559 immediate HRQoL gain is necessary to counterbalance them and, among 90-year-olds  
 1560 (especially where BCVA is good in both eyes and risk of visual loss is high), the gain would  
 1561 have to be of at least 'moderate' magnitude to make 'immediate surgery' cost effective  
 1562 compared with 'no surgery' or 'delayed surgery' (Figure 39, Figure 40). Again, we emphasise  
 1563 that this is a non-reference-case sensitivity analysis (see J.4.2.4 for discussion).

#### 1564 **Alternative – 6/9 – threshold for delayed surgery**

1565 In our sensitivity analysis exploring the impact of a 6/9 threshold for delayed surgery, we  
 1566 found that 'immediate surgery' remained optimal in most cases, even if it confers no  
 1567 immediate HRQoL benefit. There are some scenarios among 90-year-olds for which 'delayed  
 1568 (6/9) surgery' represents a better balance of benefits and costs unless it can be assumed  
 1569 that surgery will make a difference to the patient's HRQoL that can be categorised as 'very  
 1570 small'. In all these cases, risk of visual loss is raised and/or BCVA in both eyes is unimpaired.  
 1571 A full results matrix for the second-eye decision-problem is shown in Figure 43 in  
 1572 Subappendix Jd.

#### 1573 **Higher costs of cataract surgery**

1574 For second eyes, the effect is similar to that observed in first-eyes but in all cases of 90 year  
 1575 olds at any level of risk when acuity is 6/6 in both eyes a "very small" benefit is required. This  
 1576 pattern is also observed in the comparison between immediate and delayed surgery for  
 1577 second eyes.

1578

## 1579 **J.5 Discussion**

### 1580 **J.5.1.1 Principal findings**

1581 For a large majority of patients with symptomatic cataract, it is clearly optimal to offer  
 1582 surgery, and it is not cost effective to delay this until a VA threshold is met. This is true  
 1583 whether for first- or second-eye surgery. For some combinations of characteristics (typically  
 1584 relating to older patients with a high risk of perioperative visual loss), an expectation of  
 1585 improved quality of life is necessary to make surgery cost effective but, in all such cases, the  
 1586 magnitude of anticipated gain must only of 'very small' to justify immediate surgery.

1587 This model suggests that for the majority of cases delaying surgery until a visual acuity  
 1588 threshold is reached is sub-optimal, will result in a potentially avoidable loss of QALYs, and  
 1589 possibly increase costs by raising the demand for low vision support services, relative to  
 1590 offering immediate surgery. Age is a risk factor for both PCR and visual loss, and therefore  
 1591 delaying surgery is likely to increase risks of poor outcome in older people. This applies in  
 1592 the context of both first and second eyes.

1593

### 1594 **J.5.1.2 Strengths of the analysis**

1595 This model represents a means of generating evidence to aid decision makers where  
 1596 previously no similar evidence existed in the literature. The model draws on research carried  
 1597 out on large, directly applicable registry databases and is the first cataract health economic  
 1598 model to employ natural history data to simulate the visual acuity changes in **both** phakic  
 1599 and pseudophakic eyes pre and post-surgery. The model also synthesises resource use and  
 1600 cost data from RCTs, previously conducted economic analyses, NHS Reference Costs, and  
 1601 the input of the guideline committee to produce a very detailed costing of cataract surgery  
 1602 which adds to the robustness of the conclusions.



1603 We were able to use a large published, NHS based, peer-reviewed registry (the RCOphth  
1604 NOD) to parameterise probabilities of visual loss, and posterior capsular rupture. This is the  
1605 first time this data has been deployed in a health-economic model of cataract surgery. The  
1606 NOD is a live dataset so should the multivariate logistic regression models we incorporate be  
1607 updated and published, our model framework is flexible and could be updated with any new  
1608 analyses.

1609 We acknowledge the ongoing difficulty of using established HRQoL measures, beyond visual  
1610 acuity, to quantify both the morbidity caused by cataract and the effectiveness of surgery. We  
1611 have developed an approach that avoids these complications by instead postulating what  
1612 magnitude of expected HRQoL gain is necessary, given a variety of premises, for cataract  
1613 surgery to be cost-effective compared with delayed, or no surgery. We have provided some  
1614 context for these expected levels of benefit with reference to a newer index of HRQoL, the  
1615 VFQ-UI. Future research, validating HRQoL measures in populations with cataract, would  
1616 provide further context for our results.

1617 This model represents the first attempt to evaluate the cost-effectiveness of potential visual  
1618 acuity thresholds in cataract surgery. One of the central rationales for this model and the  
1619 prioritising of the relevant review questions for economic analyses was the committee  
1620 concerns about how cataract could be rationed by imposing visual acuity thresholds for  
1621 referral where no evidence exists to support their use. This model has explicitly compared  
1622 strategies of immediate surgery, delayed surgery using two potential thresholds, and a no  
1623 surgery option. In the majority of iterations the model shows that immediate surgery, whether  
1624 for first or second eyes, is optimal compared to delaying surgery.

### 1625 **J.5.1.3 Weaknesses of the analysis**

1626 Whilst the model structure presents an advantageous departure from the typical engineering  
1627 of health economic decision models, this is also a weakness as the model does not lend  
1628 itself to a thoroughgoing sensitivity analysis. Although, the utility of any probabilistic  
1629 sensitivity analysis in the context of this model structure is debatable. It may be possible to  
1630 use PSA to describe credible intervals for the utility values populating the result matrices, but  
1631 these values are already smoothed by the categorisation described in section J.3.4, and it is  
1632 likely that presenting (and interpreting) such data would be a significant challenge with  
1633 unclear benefits for the clarity of the conclusions drawn. However, the lack of a concise  
1634 statistical explanation of the uncertainty in the model, beyond the confidence limits for  
1635 parameters described in this document and the deterministic sensitivity analyses detailed in  
1636 section J.3.5 , remains a limitation.

1637 It remains a significant challenge to contextualise the HRQoL categories used by the model  
1638 with reference to specific HRQoL instruments, as all such instruments are flawed when  
1639 applied to the task of measuring the HRQoL impact of cataract and the effectiveness of  
1640 surgery in QALY terms. Further work is needed in this regard to help the general  
1641 quantification of HRQoL in cataract but also to help communicate the results of our model to  
1642 patients and practitioners by providing realistic vignettes of what a “small” gain in HRQoL for  
1643 a patient with cataract might mean in terms of survey response.

1644 There is considerable uncertainty in our understanding of how cataract develops over time,  
1645 what the consequences are in terms of VA and HRQoL, and the rate at which these  
1646 consequences manifest. Despite an extensive search of the literature, we were forced to rely  
1647 on two Scandanavian cohort studies to parameterise the visual acuity impacts of cataract  
1648 and the natural history of phackic/pseudophakic first and fellow-eyes. A complete, unbiased  
1649 understanding of this problem could only be gained via a large, randomised controlled trial  
1650 whereby patients are assigned to immediate, delayed or no surgery arms and followed up  
1651 over regular intervals for the remainder of their life expectancy. For obvious ethical reasons  
1652 this study will never take place. It is hoped that ophthalmology databases in the NHS setting

1653 may in future contain longer-term follow-up data on pseudophakic eyes and fellow-eyes  
1654 which will aid in part to addressing this weakness in the richness of data available currently.

#### 1655 J.5.1.4 Comparison with other CUAs

1656 It is clear from previously published economic evaluations that there is variation in the  
1657 calculated ICERs for first and second-eye surgery, although in all published studies the base-  
1658 case analyses suggest that surgery is cost-effective at a threshold value of £20,000 per  
1659 QALY when a lifetime perspective is taken (Table 39). One of the possible reasons for the  
1660 relatively large ICERs given the low cost of cataract surgery is the use of HRQoL tools such  
1661 as the EQ-5D which may not have the sensitivity to detect the benefits of surgery. Unlike our  
1662 model, none of the analyses published to date have attempted to model the decline in visual  
1663 acuity experienced by people with cataract and have therefore significantly overvalued no-  
1664 surgery strategies and underestimated the harms of visual loss. In our model, we incorporate  
1665 additional mortality hazards associated with visual impairment and additional NHS/PSS costs  
1666 of low vision services, and this combined with the simulation of visual acuity decline means  
1667 that our model represents a more robust analysis of the consequences of no surgery/delayed  
1668 surgery strategies than those published before, and more completely reflect the benefits and  
1669 savings associated with immediate surgery. Our model also improves upon previous  
1670 analyses by using a large, UK specific database (RCOphth NOD) of cataract surgery  
1671 outcomes and risk factors for visual loss, rather than a single trial or single centre cohort,  
1672 which may make our model more directly relevant to the NHS setting.

1673

1674

**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 <sup>nd</sup> 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 $\geq$ 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 $\geq$ 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

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## 1676 J.6 Conclusions

1677 We present a model of first and second eye cataract surgery comparing immediate, delayed  
 1678 and no surgery treatment options. The model represents a departure from the typically  
 1679 employed economic modelling approaches in NICE Guidelines and the wider literature, but  
 1680 The model results suggest that for the majority of patients presenting for cataract surgery,  
 1681 immediate surgery may be the most cost-effective strategy even if it infers no, or only very  
 1682 small, immediate HRQoL benefit. In the vast majority of modelled situations, delaying surgery  
 1683 until a visual acuity threshold is met is sub-optimal by comparison. These findings are  
 1684 broadly robust to well-defined but limited sensitivity analyses on costs, progression rates,  
 1685 and acuity thresholds which enact small changes to the results as expected but do not  
 1686 substantially change the conclusions drawn from the model.

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# 1814 Subappendix Jb – Example patient

# 1815 profiles: risk of PCR and visual loss

## 1816 Jb.1 Risk of PCR and visual loss

1817 For generating results for multiple scenarios (see J.3.4), we classified risk of PCR and risk of  
 1818 visual loss into three categories: low, moderate and high, which we defined as 0.02, 0.06 and  
 1819 0.15, respectively, for both outcomes. The model is not fundamentally tied to any way of  
 1820 estimating these risks. However, as an example of how they might be derived using the best  
 1821 published data currently available (and to elucidate how we arrived at our broad risk  
 1822 categories), the following sets out some worked examples of calculations.

1823 The best UK-specific estimates of risk of visual loss and PCR available in the literature are  
 1824 those derived from the logistic multiple regression models published by Sparrow et al. (2012)  
 1825 and Narendran et al. (2009). (see J.3.3.3 for details). We defined our risk strata on the basis  
 1826 of absolute risk estimates generated by iteratively including/excluding variables in these  
 1827 models. This was done by first developing exemplar profiles with the lowest (no risk factors)  
 1828 and highest possible (all risk factors) predictive probabilities of PCR and visual loss, and then  
 1829 observing the changes in probability between these extremes as risk factors are added or  
 1830 removed from the model. Because these covariates are on logistic scales, the absolute risks  
 1831 of PCR and visual loss in low-risk and moderate-risk categories are much lower than some  
 1832 possible values of absolute risk for those profiles with many risk factors included. This is  
 1833 reflected in the midpoints adopted for low / moderate / high probability of PCR and visual loss  
 1834 which are set at 0.02 / 0.06 / 0.15 for both. Some examples are given here to illustrate those  
 1835 levels of risk.

1836 In Table 40, the profile describes a patient of 60 years of age, with no additional  
 1837 comorbidities or risk factors other than medium-sized pupils. The probability of PCR and  
 1838 visual loss in this example falls below the threshold for low risk (0.02).

1839 **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
<b>Odds ratios for risk factors</b>			
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
<b>Calculated probability</b>			
		<b>0.019</b> <b>(Low risk)</b>	<b>0.006</b> <b>(Low risk)</b>

1840 Table 41 details a 70 year old patient with some comorbidities and an inability to lie flat  
 1841 during the cataract surgery. This combination of factors increases the probability of PCR to  
 1842 moderate, whilst the probability of visual loss is increased but remains low.

1843 **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
<b>Odds ratios for risk factors</b>			
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
<b>Calculated probability</b>			
		<b>0.061</b> (Low risk)	<b>0.014</b> (Low risk)

1844 Table 42 describes an exemplar case of 80yrs of age, with glaucoma and diabetes, a  
 1845 brunescent or white cataract which is more difficult to perform phacoemulsification on, large  
 1846 pupils, shorter axial length, is taking beta-blockers and cannot lie flat for the surgery. In this  
 1847 case the risk of PCR as evaluated by the model is described as high, and the corresponding  
 1848 likelihood of poor visual outcome is categorised as moderate.

1849 **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
<b>Odds ratios for risk factors</b>			
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
<b>Calculated probability</b>			
		<b>0.154</b> (High risk)	<b>0.086</b> (Moderate risk)

1850 Table 43 describes a patient profile with all possible comorbidities, and other risk factors at  
 1851 the worst possible level (small pupils, short axial length, unable to lie flat and taking beta  
 1852 blockers). This results in a high risk of both PCR and visual loss.

1853 **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
<b>Odds ratios for risk factors</b>			
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
<b>Calculated probability</b>			
		<b>0.740 (High risk)</b>	<b>0.383 (Moderate risk)</b>

1854 **Formulae for calculating the probability of PCR:**

1855 
$$O_{PCR} = x \prod OR_{PCR}$$

1856 
$$P_{PCR} = \frac{O_{PCR}}{1 + O_{PCR}}$$

1857 Where:

1858  $O_{PCR}$  = odds of PCR

1859  $OR_{PCR}$  = odds ratios for risk factors

1860  $x$  = Constant term (intercept from risk of PCR model [odds on natural scale])

1861  $P_{PCR}$  = probability of PCR

1862 **Formulae for calculating probability of visual loss:**

1863 
$$O_{VL|noPCR} = y \prod OR_{VL}$$

1864 
$$P_{VL|noPCR} = \frac{O_{VL|noPCR}}{1 + O_{VL|noPCR}}$$



1865

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

1866

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

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

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Where:

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

1870

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

1871

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

1872

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

1873

$O_{VL}$  = Odds of visual loss

1874

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

1875

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

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

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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:

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- 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 → 1
  - OR
  - b) moving from 2 → 1 in at least TWO separate categories.
- A **large** change is any change larger than this

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These criteria equate to utility ranges of:

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

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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.

1909 **Jc.1** Very small

VFQul 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>	<b>Extreme Difficulty</b>
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>

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

1913 **Jc.2** Small

VFQul 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>	<b>Extreme Difficulty</b>
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>	<b>A little of the time</b>
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>

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

1917 **Jc.3 Moderate**

VFQul 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>

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

1921 **Jc.4 Large**

VFQul 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>

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

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

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1927



		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			Risk of PCR			Risk of PCR		
		Low	Med	High	Low	Med	High	Low	Med	High
Age 60	Index eye 6/6	Fellow eye 6/6			Fellow eye 6/9			Fellow eye 6/12		
		Low	Med	High	Low	Med	High	Low	Med	High
	Index eye 6/9	Fellow eye 6/6			Fellow eye 6/9			Fellow eye 6/12		
		Low	Med	High	Low	Med	High	Low	Med	High
	Index eye 6/12	Fellow eye 6/6			Fellow eye 6/9			Fellow eye 6/12		
		Low	Med	High	Low	Med	High	Low	Med	High
Index eye 6/24	Fellow eye 6/6			Fellow eye 6/9			Fellow eye 6/12			
	Low	Med	High	Low	Med	High	Low	Med	High	
Age 75	Index eye 6/6	Fellow eye 6/6			Fellow eye 6/9			Fellow eye 6/12		
		Low	Med	High	Low	Med	High	Low	Med	High
	Index eye 6/9	Fellow eye 6/6			Fellow eye 6/9			Fellow eye 6/12		
		Low	Med	High	Low	Med	High	Low	Med	High
	Index eye 6/12	Fellow eye 6/6			Fellow eye 6/9			Fellow eye 6/12		
		Low	Med	High	Low	Med	High	Low	Med	High
Index eye 6/24	Fellow eye 6/6			Fellow eye 6/9			Fellow eye 6/12			
	Low	Med	High	Low	Med	High	Low	Med	High	
Age 90	Index eye 6/6	Fellow eye 6/6			Fellow eye 6/9			Fellow eye 6/12		
		Low	Med	High	Low	Med	High	Low	Med	High
	Index eye 6/9	Fellow eye 6/6			Fellow eye 6/9			Fellow eye 6/12		
		Low	Med	High	Low	Med	High	Low	Med	High
	Index eye 6/12	Fellow eye 6/6			Fellow eye 6/9			Fellow eye 6/12		
		Low	Med	High	Low	Med	High	Low	Med	High
Index eye 6/24	Fellow eye 6/6			Fellow eye 6/9			Fellow eye 6/12			
	Low	Med	High	Low	Med	High	Low	Med	High	

**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 27: Base-case results matrix – first-eye immediate -v- delayed surgery (threshold 6/12)

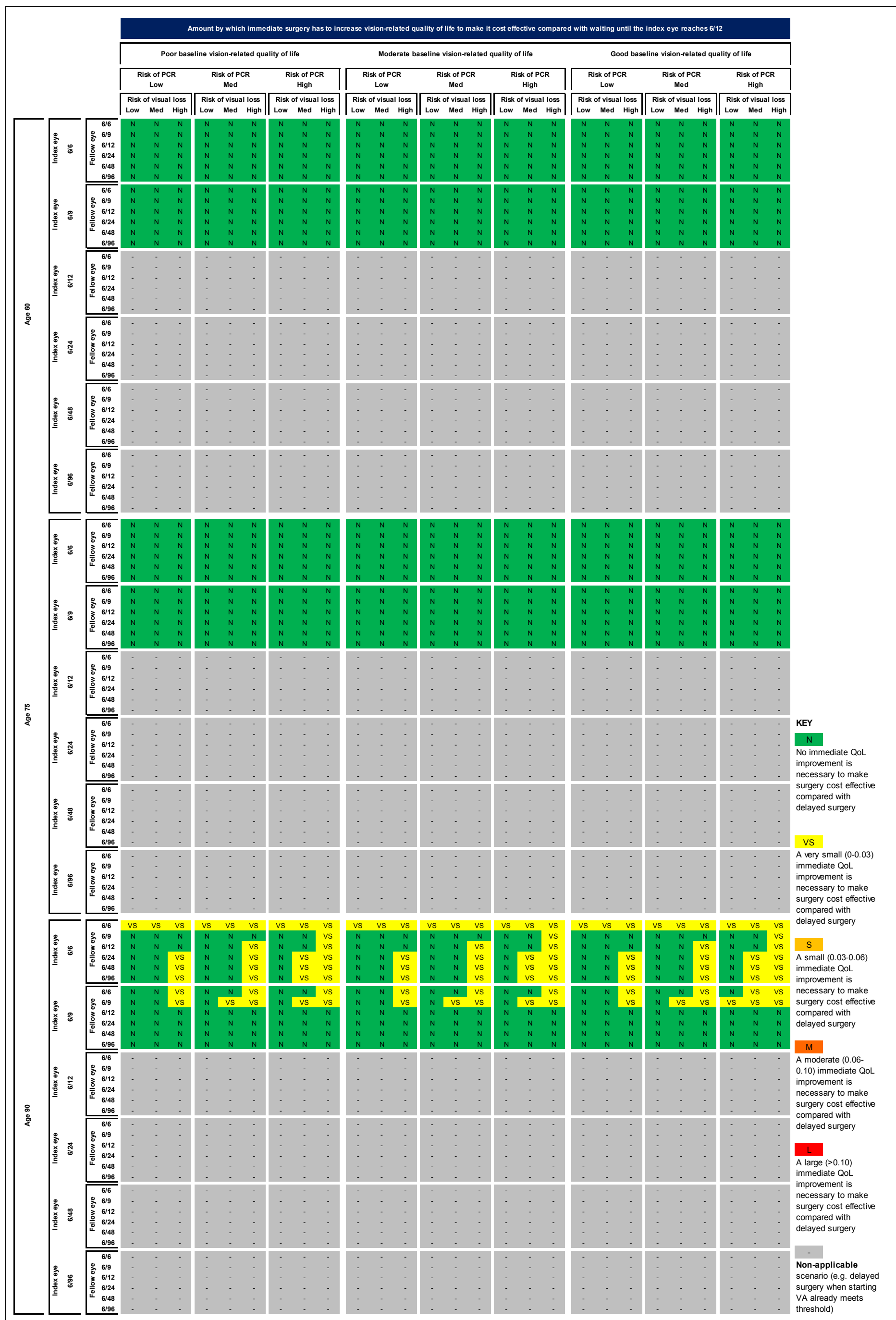
Amount by which surgery has to increase vision-related quality of life to make it cost effective compared with no surgery																								
Age	Index eye	Fellow eye	Poor baseline vision-related quality of life			Moderate baseline vision-related quality of life			Good baseline vision-related quality of life															
			Risk of PCR			Risk of PCR			Risk of PCR															
			Low	Med	High	Low	Med	High	Low	Med	High													
			Risk of visual loss	Risk of visual loss	Risk of visual loss	Risk of visual loss	Risk of visual loss	Risk of visual loss	Risk of visual loss	Risk of visual loss	Risk of visual loss													
Low Med High																								
Age 80	6/6	6/6	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	
			6/9	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
			6/12	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
	6/24	6/24	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	
			6/48	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	
			6/96	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	
	6/48	6/48	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	
			6/9	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	
			6/12	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	
	6/96	6/96	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	
			6/12	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	
			6/24	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	
	Age 75	6/6	6/6	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
				6/9	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
				6/12	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
		6/24	6/24	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
				6/48	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
				6/96	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
6/48		6/48	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	
			6/9	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	
			6/12	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	
6/96		6/96	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	
			6/12	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	
			6/24	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	
Age 90		6/6	6/6	VS	VS	VS	VS	VS	VS	VS	VS	VS	VS	VS	VS	VS	VS	VS	VS	VS	VS	VS	VS	
				6/9	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
				6/12	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
		6/24	6/24	N	N	VS	N	N	VS	N	VS	VS	N	VS	VS	N	VS	VS	N	VS	VS	N	VS	VS
				6/48	N	N	VS	N	N	VS	N	VS	VS	N	VS	VS	N	VS	VS	N	VS	VS	N	VS
				6/96	N	N	VS	N	N	VS	N	VS	VS	N	VS	VS	N	VS	VS	N	VS	VS	N	VS
	6/48	6/48	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	
			6/9	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	
			6/12	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	
	6/96	6/96	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	
			6/12	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	
			6/24	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	
	Age 85	6/6	6/6	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	
				6/9	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
				6/12	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
		6/24	6/24	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
				6/48	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
				6/96	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
6/48		6/48	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	
			6/9	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	
			6/12	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	
6/96		6/96	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	
			6/12	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	
			6/24	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 28: Base-case results matrix – second-eye immediate -v- no surgery





**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 29: Base-case results matrix – second-eye immediate -v- delayed surgery (threshold 6/12)



		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	6/9	6/12	6/6	6/9	6/12	6/6	6/9	6/12	6/6	6/9	6/12	6/6	6/9	6/12	6/6	6/9	6/12	6/6	6/9	6/12	6/6	6/9	6/12	6/6	6/9	6/12	6/6	6/9	6/12	6/6	6/9	6/12																	
		Fellow eye		6/24	6/48	6/96	6/24	6/48	6/96	6/24	6/48	6/96	6/24	6/48	6/96	6/24	6/48	6/96	6/24	6/48	6/96	6/24	6/48	6/96	6/24	6/48	6/96	6/24	6/48	6/96	6/24	6/48	6/96	6/24	6/48	6/96	6/24	6/48	6/96														
		Fellow eye		6/96	6/96	6/96	6/96	6/96	6/96	6/96	6/96	6/96	6/96	6/96	6/96	6/96	6/96	6/96	6/96	6/96	6/96	6/96	6/96	6/96	6/96	6/96	6/96	6/96	6/96	6/96	6/96	6/96	6/96	6/96	6/96	6/96	6/96	6/96	6/96														
	Age 65	Index eye 6/9	Fellow eye		6/6	6/9	6/12	6/6	6/9	6/12	6/6	6/9	6/12	6/6	6/9	6/12	6/6	6/9	6/12	6/6	6/9	6/12	6/6	6/9	6/12	6/6	6/9	6/12	6/6	6/9	6/12	6/6	6/9	6/12	6/6	6/9	6/12	6/6	6/9	6/12													
			Fellow eye		6/24	6/48	6/96	6/24	6/48	6/96	6/24	6/48	6/96	6/24	6/48	6/96	6/24	6/48	6/96	6/24	6/48	6/96	6/24	6/48	6/96	6/24	6/48	6/96	6/24	6/48	6/96	6/24	6/48	6/96	6/24	6/48	6/96	6/24	6/48	6/96	6/24	6/48	6/96										
			Fellow eye		6/96	6/96	6/96	6/96	6/96	6/96	6/96	6/96	6/96	6/96	6/96	6/96	6/96	6/96	6/96	6/96	6/96	6/96	6/96	6/96	6/96	6/96	6/96	6/96	6/96	6/96	6/96	6/96	6/96	6/96	6/96	6/96	6/96	6/96	6/96	6/96	6/96	6/96	6/96										
		Age 70	Index eye 6/12	Fellow eye		6/6	6/9	6/12	6/6	6/9	6/12	6/6	6/9	6/12	6/6	6/9	6/12	6/6	6/9	6/12	6/6	6/9	6/12	6/6	6/9	6/12	6/6	6/9	6/12	6/6	6/9	6/12	6/6	6/9	6/12	6/6	6/9	6/12	6/6	6/9	6/12	6/6	6/9	6/12									
				Fellow eye		6/24	6/48	6/96	6/24	6/48	6/96	6/24	6/48	6/96	6/24	6/48	6/96	6/24	6/48	6/96	6/24	6/48	6/96	6/24	6/48	6/96	6/24	6/48	6/96	6/24	6/48	6/96	6/24	6/48	6/96	6/24	6/48	6/96	6/24	6/48	6/96	6/24	6/48	6/96	6/24	6/48	6/96						
				Fellow eye		6/96	6/96	6/96	6/96	6/96	6/96	6/96	6/96	6/96	6/96	6/96	6/96	6/96	6/96	6/96	6/96	6/96	6/96	6/96	6/96	6/96	6/96	6/96	6/96	6/96	6/96	6/96	6/96	6/96	6/96	6/96	6/96	6/96	6/96	6/96	6/96	6/96	6/96	6/96	6/96	6/96	6/96						
			Age 75	Index eye 6/24	Fellow eye		6/6	6/9	6/12	6/6	6/9	6/12	6/6	6/9	6/12	6/6	6/9	6/12	6/6	6/9	6/12	6/6	6/9	6/12	6/6	6/9	6/12	6/6	6/9	6/12	6/6	6/9	6/12	6/6	6/9	6/12	6/6	6/9	6/12	6/6	6/9	6/12	6/6	6/9	6/12	6/6	6/9	6/12					
					Fellow eye		6/24	6/48	6/96	6/24	6/48	6/96	6/24	6/48	6/96	6/24	6/48	6/96	6/24	6/48	6/96	6/24	6/48	6/96	6/24	6/48	6/96	6/24	6/48	6/96	6/24	6/48	6/96	6/24	6/48	6/96	6/24	6/48	6/96	6/24	6/48	6/96	6/24	6/48	6/96	6/24	6/48	6/96	6/24	6/48	6/96		
					Fellow eye		6/96	6/96	6/96	6/96	6/96	6/96	6/96	6/96	6/96	6/96	6/96	6/96	6/96	6/96	6/96	6/96	6/96	6/96	6/96	6/96	6/96	6/96	6/96	6/96	6/96	6/96	6/96	6/96	6/96	6/96	6/96	6/96	6/96	6/96	6/96	6/96	6/96	6/96	6/96	6/96	6/96	6/96					
				Age 80	Index eye 6/48	Fellow eye		6/6	6/9	6/12	6/6	6/9	6/12	6/6	6/9	6/12	6/6	6/9	6/12	6/6	6/9	6/12	6/6	6/9	6/12	6/6	6/9	6/12	6/6	6/9	6/12	6/6	6/9	6/12	6/6	6/9	6/12	6/6	6/9	6/12	6/6	6/9	6/12	6/6	6/9	6/12	6/6	6/9	6/12				
						Fellow eye		6/24	6/48	6/96	6/24	6/48	6/96	6/24	6/48	6/96	6/24	6/48	6/96	6/24	6/48	6/96	6/24	6/48	6/96	6/24	6/48	6/96	6/24	6/48	6/96	6/24	6/48	6/96	6/24	6/48	6/96	6/24	6/48	6/96	6/24	6/48	6/96	6/24	6/48	6/96	6/24	6/48	6/96	6/24	6/48	6/96	
						Fellow eye		6/96	6/96	6/96	6/96	6/96	6/96	6/96	6/96	6/96	6/96	6/96	6/96	6/96	6/96	6/96	6/96	6/96	6/96	6/96	6/96	6/96	6/96	6/96	6/96	6/96	6/96	6/96	6/96	6/96	6/96	6/96	6/96	6/96	6/96	6/96	6/96	6/96	6/96	6/96	6/96	6/96	6/96				
					Age 85	Index eye 6/96	Fellow eye		6/6	6/9	6/12	6/6	6/9	6/12	6/6	6/9	6/12	6/6	6/9	6/12	6/6	6/9	6/12	6/6	6/9	6/12	6/6	6/9	6/12	6/6	6/9	6/12	6/6	6/9	6/12	6/6	6/9	6/12	6/6	6/9	6/12	6/6	6/9	6/12	6/6	6/9	6/12	6/6	6/9	6/12			
							Fellow eye		6/24	6/48	6/96	6/24	6/48	6/96	6/24	6/48	6/96	6/24	6/48	6/96	6/24	6/48	6/96	6/24	6/48	6/96	6/24	6/48	6/96	6/24	6/48	6/96	6/24	6/48	6/96	6/24	6/48	6/96	6/24	6/48	6/96	6/24	6/48	6/96	6/24	6/48	6/96	6/24	6/48	6/96	6/24	6/48	6/96
							Fellow eye		6/96	6/96	6/96	6/96	6/96	6/96	6/96	6/96	6/96	6/96	6/96	6/96	6/96	6/96	6/96	6/96	6/96	6/96	6/96	6/96	6/96	6/96	6/96	6/96	6/96	6/96	6/96	6/96	6/96	6/96	6/96	6/96	6/96	6/96	6/96	6/96	6/96	6/96	6/96	6/96	6/96	6/96			

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- 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 31: Sensitivity analysis (unrelated future costs, first year only) – results matrix – first-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														
		Low	Med	High	Low	Med	High	Low	Med	High	Low	Med	High	Low	Med	High	Low	Med	High	Low	Med	High	Low	Med	High	Low	Med	High												
Age 60	Index eye 6/6	Fellow eye 6/6			Fellow eye 6/9			Fellow eye 6/12			Fellow eye 6/24			Fellow eye 6/48			Fellow eye 6/96			Fellow eye 6/6			Fellow eye 6/9			Fellow eye 6/12			Fellow eye 6/24			Fellow eye 6/48			Fellow eye 6/96					
		Age 75	Index eye 6/6	Fellow eye 6/6			Fellow eye 6/9			Fellow eye 6/12			Fellow eye 6/24			Fellow eye 6/48			Fellow eye 6/96			Fellow eye 6/6			Fellow eye 6/9			Fellow eye 6/12			Fellow eye 6/24			Fellow eye 6/48			Fellow eye 6/96			
				Age 90	Index eye 6/6	Fellow eye 6/6			Fellow eye 6/9			Fellow eye 6/12			Fellow eye 6/24			Fellow eye 6/48			Fellow eye 6/96			Fellow eye 6/6			Fellow eye 6/9			Fellow eye 6/12			Fellow eye 6/24			Fellow eye 6/48			Fellow eye 6/96	

**KEY**

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- 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**

		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	N N N									N N N									N N N								
		Fellow eye 6/9	N N N									N N N									N N N								
		Fellow eye 6/12	N N N									N N N									N N N								
	Index eye 6/9	Fellow eye 6/6	N N N									N N N									N N N								
		Fellow eye 6/9	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 6/12	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	N N N									N N N									N N N								
		Fellow eye 6/9	N N N									N N N									N N N								
		Fellow eye 6/12	N N N									N N N									N N N								
	Index eye 6/9	Fellow eye 6/6	N N N									N N N									N N N								
		Fellow eye 6/9	VS VS VS			VS VS VS			VS VS VS			VS VS VS			VS VS VS			VS VS VS			VS VS VS								
		Fellow eye 6/12	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	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	VS VS VS			VS VS VS			VS VS VS			VS VS VS			VS VS VS			VS VS VS			VS VS VS								
		Fellow eye 6/12	VS VS VS									VS VS VS									VS VS VS								
	Index eye 6/9	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								
		Fellow eye 6/9	VS VS VS			VS VS VS			VS VS VS			VS VS VS			VS VS VS			VS VS VS			VS VS VS								
		Fellow eye 6/12	VS VS VS									VS VS VS									VS VS VS								
	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 35: Sensitivity analysis (cost of cataract surgery increased by £500) – results matrix – first-eye immediate -v- delayed surgery (threshold 6/12)

		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 6/9																														
		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						
		Index eye	Fellow eye	Index eye	Fellow eye	Index eye	Fellow eye	Index eye	Fellow eye	Index eye	Fellow eye	Index eye	Fellow eye	Index eye	Fellow eye	Index eye	Fellow eye	Index eye	Fellow eye	Index eye	Fellow eye	Index eye	Fellow eye	Index eye	Fellow eye	Index eye	Fellow eye					
		Age 60		6/6	6/6	6/9	6/12	6/24	6/48	6/96	6/6	6/9	6/12	6/24	6/48	6/96	6/6	6/9	6/12	6/24	6/48	6/96	6/6	6/9	6/12	6/24	6/48	6/96	6/6	6/9	6/12	6/24
		[Matrix cells with values N, VS, S, M, L, or -]																														
		[Matrix cells with values N, VS, S, M, L, or -]																														
		[Matrix cells with values N, VS, S, M, L, or -]																														
		[Matrix cells with values N, VS, S, M, L, or -]																														
		[Matrix cells with values N, VS, S, M, L, or -]																														
		[Matrix cells with values N, VS, S, M, L, or -]																														
		[Matrix cells with values N, VS, S, M, L, or -]																														
		[Matrix cells with values N, VS, S, M, L, or -]																														
		[Matrix cells with values N, VS, S, M, L, or -]																														
		[Matrix cells with values N, VS, S, M, L, or -]																														
		[Matrix cells with values N, VS, S, M, L, or -]																														
		[Matrix cells with values N, VS, S, M, L, or -]																														
		[Matrix cells with values N, VS, S, M, L, or -]																														
		[Matrix cells with values N, VS, S, M, L, or -]																														
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		[Matrix cells with values N, VS, S, M, L, or -]																														
		[Matrix cells with values N, VS, S, M, L, or -]																														
		[Matrix cells with values N, VS, S, M, L, or -]																														
		[Matrix cells with values N, VS, S, M, L, or -]																														
		[Matrix cells with values N, VS, S, M, L, or -]																														
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		[Matrix cells with values N, VS, S, M, L, or -]																														
		[Matrix cells with values N, VS, S, M, L, or -]																														
		[Matrix cells with values N, VS, S, M, L, or -]																														

**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 36: Sensitivity analysis (alternative acuity threshold for delayed surgery) – results matrix – first-eye immediate -v- delayed surgery (threshold 6/9)**







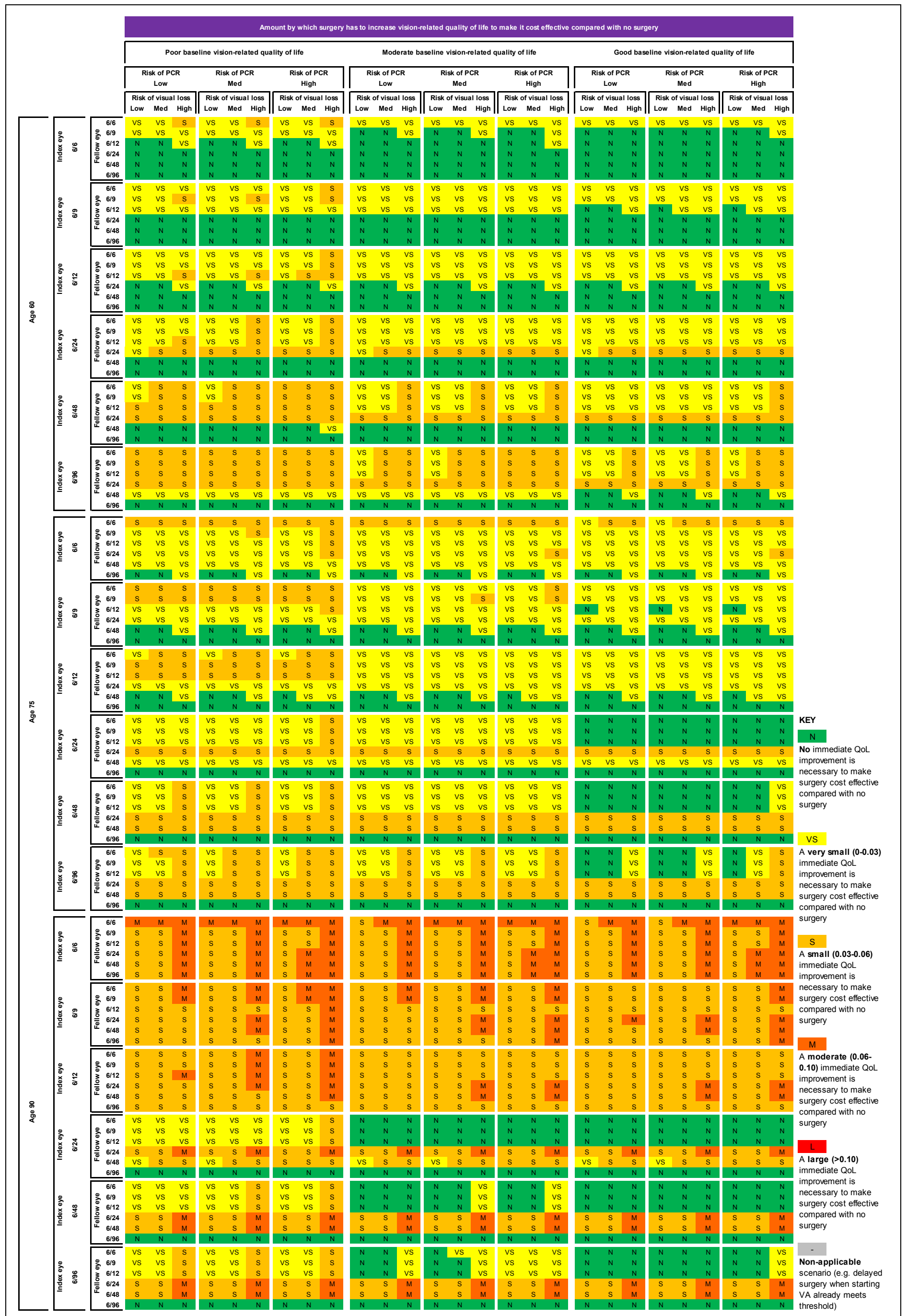


Figure 39: Sensitivity analysis (unrelated future costs, all years) – results matrix – second-eye immediate -v- no surgery

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 visual loss Low	Risk of visual loss Med	Risk of visual loss High	Risk of visual loss Low	Risk of visual loss Med	Risk of visual loss High	Risk of visual loss Low	Risk of visual loss Med	Risk of visual loss High	Risk of visual loss Low	Risk of visual loss Med	Risk of visual loss High	
Age 60	Index eye 6/6	6/6	VS	VS	S	VS	VS	S	VS	VS	S	VS	VS	S
		6/9	N	N	N	N	N	N	N	N	N	N	N	N
	Index eye 6/9	6/12	N	N	N	N	N	N	N	N	N	N	N	N
		6/24	N	N	N	N	N	N	N	N	N	N	N	N
	Index eye 6/12	6/48	N	N	N	N	N	N	N	N	N	N	N	N
		6/96	N	N	N	N	N	N	N	N	N	N	N	N
Age 75	Index eye 6/6	6/6	S	S	S	S	S	S	S	S	S	S	S	
		6/9	N	VS	VS	N	VS	VS	N	VS	VS	N	VS	VS
	Index eye 6/9	6/12	N	N	N	N	N	N	N	N	N	N	N	N
		6/24	N	N	N	N	N	N	N	N	N	N	N	N
	Index eye 6/12	6/48	N	N	N	N	N	N	N	N	N	N	N	N
		6/96	N	N	N	N	N	N	N	N	N	N	N	N
Age 90	Index eye 6/6	6/6	M	M	M	M	M	M	M	M	M	M	M	
		6/9	S	S	M	S	S	M	S	S	M	S	S	M
	Index eye 6/9	6/12	S	S	M	S	S	M	S	S	M	S	S	M
		6/24	S	S	M	S	S	M	S	S	M	S	S	M
	Index eye 6/12	6/48	S	S	M	S	S	M	S	S	M	S	S	M
		6/96	S	S	M	S	S	M	S	S	M	S	S	M

**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)**

1947  
1948



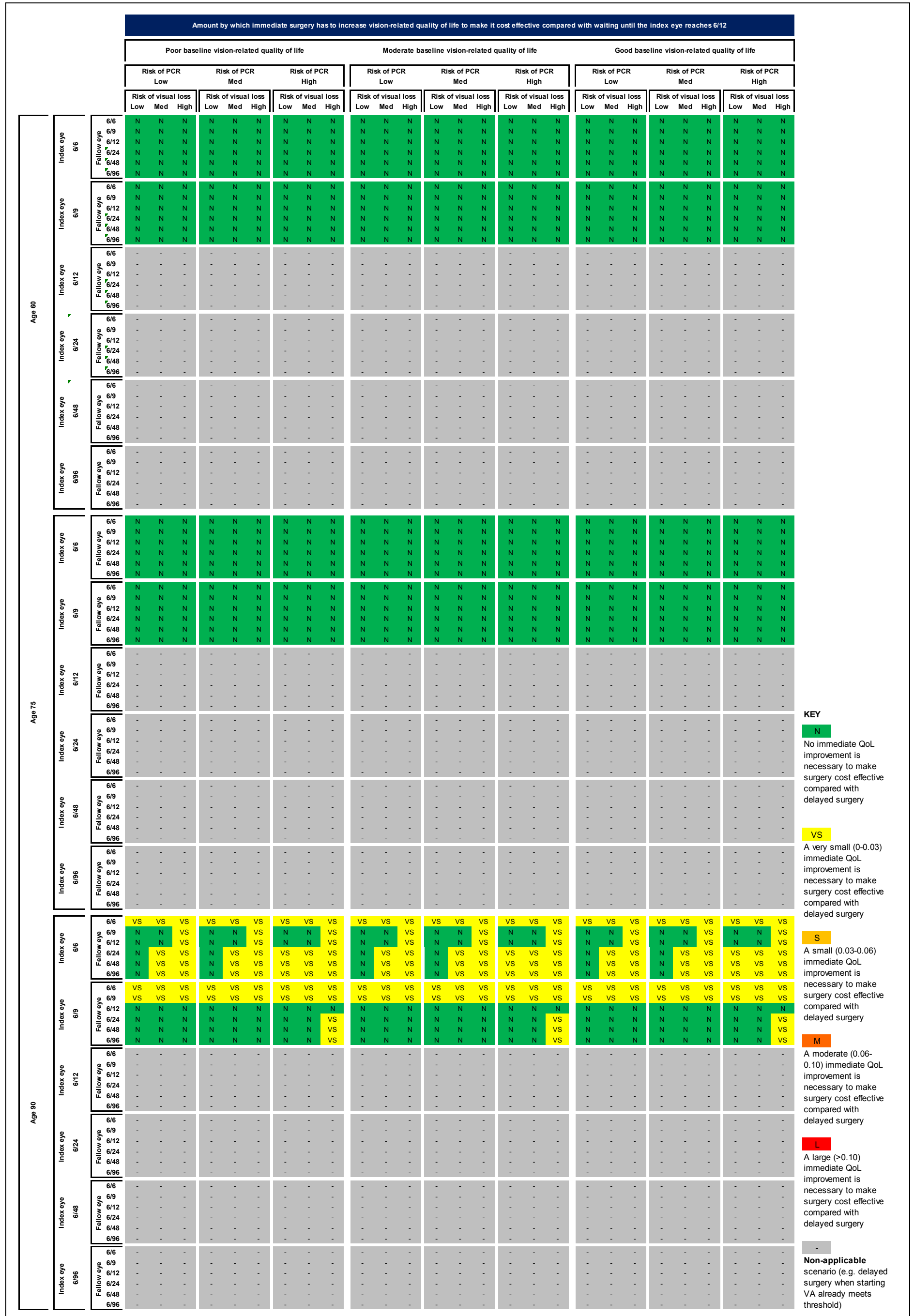


Figure 42: Sensitivity analysis (cost of cataract surgery increased by £500) – results matrix – second-eye immediate -v- delayed surgery (threshold 6/12)

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 6/9

	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 6/9																																						
	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														
	Low	Med	High	Low	Med	High	Low	Med	High	Low	Med	High	Low	Med	High	Low	Med	High	Low	Med	High	Low	Med	High	Low	Med	High												
Age 60	Index eye 6/6			Follow eye 6/6			Follow eye 6/9			Follow eye 6/12			Follow eye 6/24			Follow eye 6/48			Follow eye 6/96			Follow eye 6/6			Follow eye 6/9			Follow eye 6/12			Follow eye 6/24			Follow eye 6/48			Follow eye 6/96		
				Index eye 6/6			Follow eye 6/6			Follow eye 6/9			Follow eye 6/12			Follow eye 6/24			Follow eye 6/48			Follow eye 6/96			Follow eye 6/6			Follow eye 6/9			Follow eye 6/12			Follow eye 6/24			Follow eye 6/48		
	Index eye 6/9						Follow eye 6/6			Follow eye 6/9			Follow eye 6/12			Follow eye 6/24			Follow eye 6/48			Follow eye 6/96			Follow eye 6/9			Follow eye 6/12			Follow eye 6/24			Follow eye 6/48			Follow eye 6/96		
				Index eye 6/12			Follow eye 6/6			Follow eye 6/9			Follow eye 6/12			Follow eye 6/24			Follow eye 6/48			Follow eye 6/96			Follow eye 6/12			Follow eye 6/12			Follow eye 6/24			Follow eye 6/48			Follow eye 6/96		
	Index eye 6/24						Follow eye 6/6			Follow eye 6/9			Follow eye 6/12			Follow eye 6/24			Follow eye 6/48			Follow eye 6/96			Follow eye 6/24			Follow eye 6/24			Follow eye 6/48			Follow eye 6/96					
				Index eye 6/48			Follow eye 6/6			Follow eye 6/9			Follow eye 6/12			Follow eye 6/24			Follow eye 6/48			Follow eye 6/96			Follow eye 6/48			Follow eye 6/48			Follow eye 6/96			Follow eye 6/96					
	Index eye 6/96						Follow eye 6/6			Follow eye 6/9			Follow eye 6/12			Follow eye 6/24			Follow eye 6/48			Follow eye 6/96			Follow eye 6/96			Follow eye 6/96			Follow eye 6/96			Follow eye 6/96			Follow eye 6/96		
				Index eye 6/6			Follow eye 6/6			Follow eye 6/9			Follow eye 6/12			Follow eye 6/24			Follow eye 6/48			Follow eye 6/96			Follow eye 6/6			Follow eye 6/9			Follow eye 6/12			Follow eye 6/24			Follow eye 6/48		
	Index eye 6/9						Follow eye 6/6			Follow eye 6/9			Follow eye 6/12			Follow eye 6/24			Follow eye 6/48			Follow eye 6/96			Follow eye 6/9			Follow eye 6/12			Follow eye 6/24			Follow eye 6/48			Follow eye 6/96		
				Index eye 6/12			Follow eye 6/6			Follow eye 6/9			Follow eye 6/12			Follow eye 6/24			Follow eye 6/48			Follow eye 6/96			Follow eye 6/12			Follow eye 6/12			Follow eye 6/24			Follow eye 6/48			Follow eye 6/96		
	Index eye 6/24						Follow eye 6/6			Follow eye 6/9			Follow eye 6/12			Follow eye 6/24			Follow eye 6/48			Follow eye 6/96			Follow eye 6/24			Follow eye 6/24			Follow eye 6/48			Follow eye 6/96					
				Index eye 6/48			Follow eye 6/6			Follow eye 6/9			Follow eye 6/12			Follow eye 6/24			Follow eye 6/48			Follow eye 6/96			Follow eye 6/48			Follow eye 6/48			Follow eye 6/96			Follow eye 6/96					
	Index eye 6/96						Follow eye 6/6			Follow eye 6/9			Follow eye 6/12			Follow eye 6/24			Follow eye 6/48			Follow eye 6/96			Follow eye 6/96			Follow eye 6/96			Follow eye 6/96			Follow eye 6/96					

**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

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**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 43: Sensitivity analysis (alternative acuity threshold for delayed surgery) – results matrix – second-eye immediate -v- delayed surgery (threshold 6/9)