RVO model, taking account of age of patients at and after a FEO

Technical Document for Model v2.04; 23 December 2010

The model submitted to NICE has been updated to take into account the age of patients at and after the time of fellow eye involvement, correcting the issue identified by the ERG. This document details these changes and results based on an amended model.

Contents

Model Changes

Take account of age at FEO only

A model which takes into account the age at the time of FEO only was provided to NICE on November 23rd. This was a simple variant of the originally submitted model, with updated formulae in CG17:DJ18 in the CRVO and BRVO worksheets. The updated formulae correctly implement the expected survival at the time of FEO, but assume that patients with FEO have the same survival as patients with an index RVO thereafter. This means that patients with an FEO have better survival than those without FEO. This model is not discussed further in this document.

Model each FEO cohort separately (so that their age is correctly taken into account)

The most straightforward implementation would require about 30 columns for each of 30 FEO sub-models for each type of RVO. The 30 FEO sub-models are for FEO occurrence one year, two years, three years, up to 30 years after original RVO.

However, the structure of the model is such that some simplification is possible. After the possible treatment period (first three years), the health states partition into HS0-4 (which has a time-dependent death rate and a time-dependent transition rate to HS5) and HS5 (which has a different time dependent death rate with no transition back to HS0-4). The cost depends on the proportion of patients alive and the proportion of patients in HS5 (since cost of vision loss occurs only for those in HS5).

This suggests collapsing the model into two health states (HS0-4 and HS5). The proportion of patients in these two health states needs to be stored for each treatment group for each FEO sub-model. The proportion surviving each cycle depends on the type of RVO, treatment group, collapsed health state and current age of the cohort (but is then not dependent on the time since FEO). The transition probability between HS0-4 and HS5 depends on treatment group and time since entry into the cohort (but not on the current age of the cohort). The cost in each cycle depends on the treatment group and proportion in the two collapsed health states. The QALY accrued in each cycle depends on the proportion and the average utility in each health state, where the average utility for HS5 is a known constant and depends on type of RVO, treatment group and time since FEO for HS0-4.

The model can also be simplified into these two collapsed health states in the first three years if there were no differential survival between HS0-4 and HS5. These calculations require the average cost and utility for the cohort over the six half-years in this three year period.

This has been implemented in four new worksheets (C_Oz, C_Sh, B_Oz and B_Sh), which contain the 30 sub-models for FEO for each type of RVO and treatment group. Columns A:AB contain a copy of the model for an index BSE RVO when there is no mortality. This model is used to calculate:

- the average half-yearly cost (c′(i) in AE28:AE33, for i=½, 1, 1½, ..., 3) and half-yearly QALY increment (utility (u′(i) in AH28:AH33, for i=½, 1, 1½, ..., 3) per alive patient in the first three years after a BSE RVO

- the proportion of patients in the collapsed health states (x′(i) for the proportion in HS0-4 at half-year i [AE45:AE158], y′(i) for the proportion in HS5 at half-year i [AF45:AF158]) after the first three years after an BSE RVO

- the transition probability for HS0-4 to HS5 after three years after the FEO RVO (θ′(i) [AG45:AG158]), which is calculated from the proportions in HS0-4 and HS5 (i.e., from x′(i) and y′(i)).

- the average utility for patients in HS0-4 (u′(i) [AH45:AH158]) after the first 3 years after an BSE RVO

- the half-yearly survival of patients in HS0-4 (π(a), a = ½, 1, 1½, ... [AI39:AI158]) in each half-year after the index RVO

- the half-yearly survival of patients in HS5 (ρ(a), a = 3½, 4, 4½, ... [AJ45:AJ158]) in each half-year after the index RVO; ρ(a) has been set equal to π(a), a = ½, 1, 1½, ... ,3 to ensure that the death rates are the same for all health states in the first 3 years after the RVO occurs (this is required so that the calculations involving the collapsed health states reproduce the calculations if the health states were not collapsed)

The calculations for the model in the CRVO and BRVO worksheets have been re-arranged so that the matrix multiplications involving the transition matrices are in one set of columns (e.g. AD:AP for the WSE) and survival is consistently applied in another set of columns (e.g. K:Z for the WSE). This means that the model can accommodate mortality in the first year after an RVO and this is now a parameter (Summary!J41 = 1 (yes) or 0 (no)). Differential mortality between HS0-4 and HS5 for the first three years after an RVO is turned off (via Summary!L41 = 0 (no; the default) or 1 (yes; for which the FEO calculations will be incorrect)). The copy of the model for the BSE eye is the same in C_Oz and C_Sh and the same in B_Oz and B_Sh (with a parameter in AE23 used to choose which treatment group the worksheet is for). The model in these worksheets assumes no mortality, so the columns that apply mortality are omitted.

Columns AD:AR contain the calculation of the quantities required for the FEO sub-models. The subsequent columns are:

- AS:AV Cumulative ICERs (C_Oz and B_Oz only)

- AW:CB proportion of patients in HS0-4 over time (rows 40:158) for FEO at the end of year 1 to year 30, WSE with no FEO ever and BSE (columns)

- CC:DH proportion of patients in HS5 over time (rows 40:158) for FEO at the end of year 1 to year 30, WSE with no FEO ever and BSE (columns)

- DI:EO cumulative discounted and half-cycle corrected cost over time (rows 40:158) for FEO at the end of year 1 to year 30, WSE with no FEO ever, WSE with or without FEO and BSE (columns)

- EP:FV cumulative discounted and half-cycle corrected QALY over time (rows 40:158) for FEO at the end of year 1 to year 30, WSE with no FEO ever, WSE with or without FEO and BSE (columns)

The end of each half-year is given in column AS.

The FEO sub-models (e.g. columns AW:BZ) have a formula in the 'top-left' cell that has been dragged down and across. The formula has three parts, using the WSE model (values in column CA, for example) until the time of FEO (which is given in row 22), using a calculation for the BSE in the first three years for the first three years after the FEO and a (simpler) formula for the BSE after the first three years after the FEO. For the cost and QALY calculations (DI40:EL158 and EP40:FS158), parts two and three of the formulae apply a weighted average of FEO being CRVO or BRVO based on the percentage of CRVO patients specified as an input parameter (Summary!D35 which has been copied to FR3 in the C_Oz, C_Sh, B_Oz and B_Sh worksheets). For the cost and QALY calculations, there is a column for the WSE without FEO (e.g. column EM) and column for WSE taking account of FEO (which is a weighted sum of the FEO sub-models in the preceding 31 columns; e.g. column EN). The last column (e.g., column EO) is for an index BSE RVO.

These calculations assume that there is no differential survival of patients in HS0-4 compared with HS5 in the first three years after an RVO. The type of RVO is the same for the index and FEO RVO when Summary!F8 is set to zero and the FEO RVO is of either type when Summary!F8 is set to one (in which case, the proportion of CRVO is given by Summary!D35).

Summary quantities from this model are shown in the Summary worksheet. The columns for the previous method of calculation of the effects of FEO in the CRVO and BRVO worksheets have been deleted.

Half-cycle correction

In addition to the above revisions, the cost and QALY calculations have been updated to make the half-cycle correction use the average of the proportions in each health state at the start and end of each cycle, rather than the average of the proportions in each health state at the end of each model cycle, before and after applying survival for that cycle. The latter approach had been used in previous versions of the model.

Because treatment is assumed to occur at the start of a cycle, the cost of treatment has not been half-cycle corrected. This affects the calculations in columns I and AT in the CRVO and BRVO worksheets and column I in the C_Oz, C_Sh, B_Oz and B_Sh worksheets.

The maintenance costs and the cost of vision loss have been half-cycle corrected, which is appropriate for costs that occur at random or uniformly throughout a model cycle. This affects the calculations in columns J, T, AU and BE in the CRVO and

BRVO worksheets and columns J and T in the C_Oz, C_Sh, B_Oz and B_Sh worksheets.

In cells J20, T20, AU20 and BE20 in the CRVO and BRVO worksheets, the initial non-Ozurdex 'treatment' cost is assumed to occur for all patients when they have their index RVO (and is therefore not half-cycle corrected) but the cost of vision loss is half-cycle corrected.

The cost calculations for the fellow-eye sub-models in columns DI:EO are also half-cycle corrected.

The QALY calculations have been half-cycle corrected. These calculations are in rows 160:180 in the CRVO and BRVO worksheets and in columns EP:FV in the C_Oz, C_Sh, B_Oz and B_Sh worksheets.

Half-cycle correction is not expected to have a large effect on the calculated cost and QALY differences. With a maximum cycle length of half a year, the proportion of patients alive at the start and end of each model cycle is similar.

Comparison of results between the updated and original models

Table 1 compares summary statistics produced the updated model and the original model submitted to NICE. The new model gives higher ICERs than the original model based on the original costs included within the submission, which is expected because even though treatment of a fellow eye RVO (BSE RVO) is more cost-effective than for the index WSE RVO, this becomes less cost-effective the older the patient is at the time of FEO.

The new version of the model has also been populated with revised costs suggested in the ERG report. The following parameters were changed:

- The cost of residential care was reduced to £16,999 (VL_Cost!E16 = 16999)
- The cost of administration was reduced to £150 (Summary!V10 = 150)
- The cost of cataract extraction was reduced to £789 (AE_Cost!F91 = 789)

Table 1: Estimated ICERs by patient population and model version

Model	All RVO	CRVO	BRVO-MH	BRVO-PL
Original	£7,368	£6,008	£7,953	Dominant
New (original cost assumptions)	£10,271	£8,165	£11,403	Dominant
New (revised cost assumptions)	£7,616	£6,221	£8,313	Dominant

Abbreviations: ICER, incremental cost-effectiveness ratio; RVO, retinal vein occlusion; CRVO, central retinal vein occlusion; BRVO, branch retinal vein occlusion; MH, macular haemorrhage; PL, previous laser.

Results (based on original costs assumptions)

Results were generated in an identical manner to that described in the original written submission. Table 2 - Table 5 and Figure 1 present summary results of cost-effectiveness assuming the same cost assumptions as the original submitted model. Appendix A presents additional results for this version of the model, including disaggregated costs and QALYS.

Table 2: All RVO (original cost assumptions)

Technologies	Total costs (£)	Total LYG	Total QALYs	Incremental costs (£)	Incremental LYG	Incremental QALYs	ICER (£) versus observation (QALYs)
Observation	£9,646	13.75	11.04	-	-	-	-
Ozurdex	£11,809	13.83	11.25	£2,163	0.08	0.21	£10,271

Table 3: CRVO (original cost assumptions)

Technologies	Total costs (£)	Total LYG	Total QALYs	Incremental costs (£)	Incremental LYG	Incremental QALYs	ICER (£) versus observation (QALYs)
Observation	£12,221	13.71	10.89	-	-	-	-
Ozurdex	£14,559	13.82	11.18	£2,338	0.11	0.29	£8,165

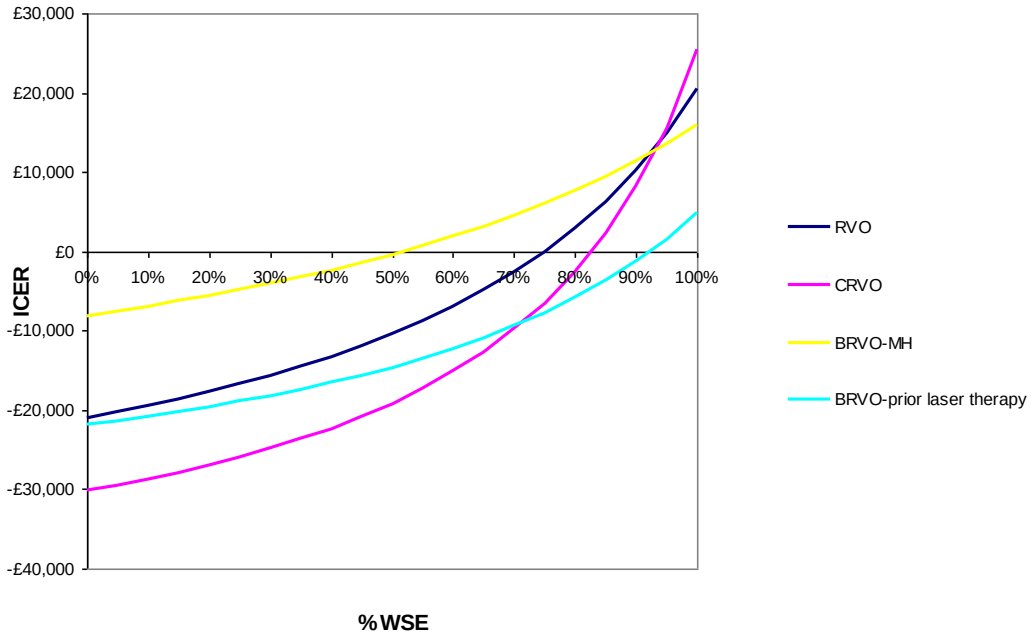
Table 4: BRVO with macular haemorrhage (original cost assumptions)

Technologies	Total costs (£)	Total LYG	Total QALYs	Incremental costs (£)	Incremental LYG	Incremental QALYs	ICER (£) versus observation (QALYs)
Observation	£8,466	13.76	11.11	-	-	-	-
Ozurdex	£10,470	13.83	11.28	£2,005	0.06	0.18	£11,403

Table 5: BRVO with previous laser (original cost assumptions)

Technologies	Total costs (£)	Total LYG	Total QALYs	Incremental costs (£)	Incremental LYG	Incremental QALYs	ICER (£) versus observation (QALYs)
Observation	£12,687	13.68	10.83	-	-	-	-
Ozurdex	£12,327	13.79	11.12	-£360	0.11	0.29	Dominant

Figure 1: Varying % WSE (original cost assumptions)



Results (based on revised costs assumptions)

Table 6 -

Table 9 and Figure 2 present summary results of cost-effectiveness assuming the revised cost assumptions of:

- Cost of residential care reduced to £16,999
- Cost of administration reduced to £150
- Cost of cataract extraction was reduced to £789

Additional disaggregated results are presented in Appendix B.

Table 6: All RVO (revised cost assumptions)

Technologies	Total costs (£)	Total LYG	Total QALYs	Incremental costs (£)	Incremental LYG	Incremental QALYs	ICER (£) versus observation (QALYs)
Observation	£7,873	13.75	11.04	-	-	-	-
Ozurdex	£9,477	13.83	11.25	£1,604	0.08	0.21	£7,616

Table 7: CRVO (revised cost assumptions)

Technologies	Total costs (£)	Total LYG	Total QALYs	Incremental costs (£)	Incremental LYG	Incremental QALYs	ICER (£) versus observation (QALYs)
Observation	£9,868	13.71	10.89	-	-	-	-
Ozurdex	£11,649	13.82	11.18	£1,782	0.11	0.29	£6,221

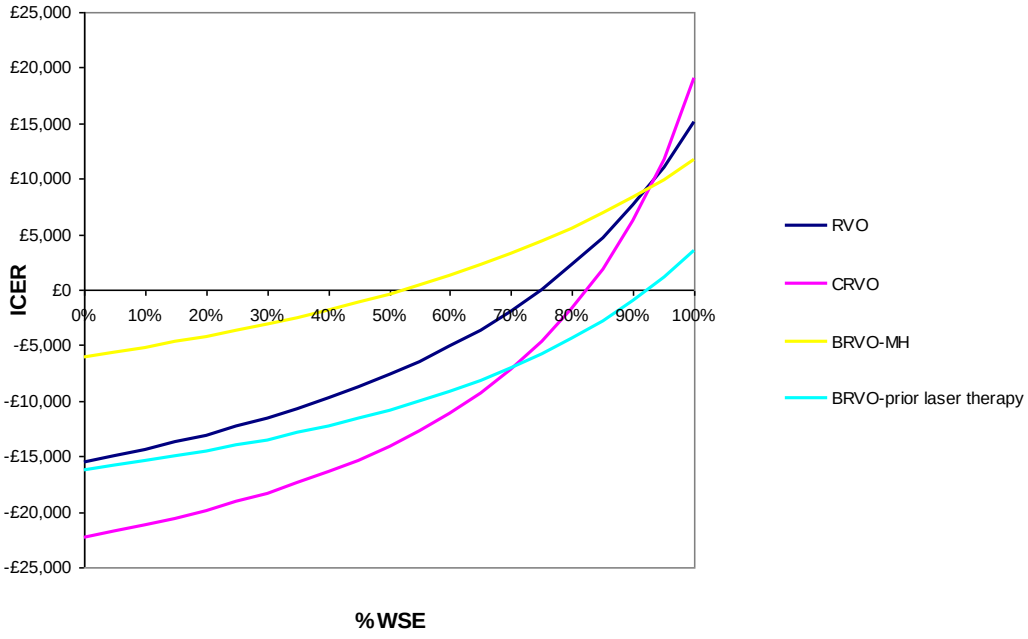
Table 8: BRVO with macular haemorrhage (revised cost assumptions)

Technologies	Total costs (£)	Total LYG	Total QALYs	Incremental costs (£)	Incremental LYG	Incremental QALYs	ICER (£) versus observation (QALYs)
Observation	£6,952	13.76	11.11	-	-	-	-
Ozurdex	£8,413	13.83	11.28	£1,461	0.06	0.18	£8,313

Table 9: BRVO with previous laser (revised cost assumptions)

Technologies	Total costs (£)	Total LYG	Total QALYs	Incremental costs (£)	Incremental LYG	Incremental QALYs	ICER (£) versus observation (QALYs)
Observation	£10,077	13.68	10.83	-	-	-	-
Ozurdex	£9,788	13.79	11.12	-£289	0.11	0.29	Dominant

Figure 2: Changes in ICER with changes in WSE:BSE ratio (revised cost assumptions)



Additional Sensitivity analyses performed by the ERG

Table 10 recreates the additional sensitivity analysis performed by the ERG starting from the original cost assumptions and introducing further revisions.

Table 10: ERG additional sensitivity analyses (Table 37 of draft ERG report)

	WSE: BSE 90%:10%			WSE: BSE 97%:03%		
Weibull FEI	CRVO	BRVO-MH	BRVO-PL	CRVO	BRVO-MH	BRVO-PL
Base case	£8,165	£11,403	Dominant	£19,210	£14,525	£2,890
1. Admin £150	£991	£3,749	Dominant	£10,573	£6,173	Dominant
2. Blindness £5,964	£13,417	£15,984	£3,627	£23,095	£18,985	£7,268
3. 1&2 & Cat. £789	£6,221	£8,313	Dominant	£14,430	£10,614	£2,053
5. 3 & age 55	£771	£2,466	Dominant	£8,077	£4,149	Dominant
6. 3 & age 75	£18,055	£21,289	£7,481	£29,079	£25,231	£11,805
	WSE: BSE 90%:10%			WSE: BSE 97%:03%		
No FEI	CRVO	BRVO-MH	BRVO-PL	CRVO	BRVO-MH	BRVO-PL
Base case	£17,606	£34,377	£12,003	£36,392	£47,711	£23,623
1. Admin £150	£9,399	£23,490	£6,206	£25,782	£34,440	£16,397
2. Blindness £5,964	£21,517	£36,144	£14,580	£37,909	£48,357	£24,587
3. 1&2 & Cat. £789	£13,282	£25,233	£8,771	£27,263	£35,057	£17,345
5. 3 & age 55	£8,195	£19,287	£5,381	£20,917	£27,725	£13,314
6. 3 & age 75	£25,427	£40,074	£16,894	£43,310	£53,571	£27,433

Appendix 4 of the draft ERG report was used to recreate the structural sensitivity analysis performed by the ERG. The base case assumes the original costs included in the original written submission and details of the revised costs used are provided in Table 16.

Table 11: ERG additional structural sensitivity analyses (Table 38 of draft ERG report)

	WSE: BSE 90%:10%			WSE: BSE 97%:03%		
Weibull FEI	CRVO	BRVO-MH	BRVO-PL	CRVO	BRVO-MH	BRVO-PL
Base case	£8,165	£11,403	Dominant	£19,210	£14,525	£2,890
Revised Obs. TPM	£17,514	£33,681	£4,657	£31,929	£35,706	£9,135
Rev. TPM & costs	£13,200	£24,708	£3,347	£23,919	£26,197	£6,651
	WSE: BSE 90%:10%			WSE: BSE 97%:03%		
No FEI	CRVO	BRVO-MH	BRVO-PL	CRVO	BRVO-MH	BRVO-PL
Base case	£17,606	£34,377	£12,003	£36,392	£47,711	£23,623
Revised Obs. TPM	£25,638	£80,920	£19,416	£47,211	£98,891	£32,060
Rev. TPM & costs	£19,292	£59,464	£14,224	£35,355	£72,685	£23,548

Sensitivity analysis: original cost assumptions

Deterministic

Univariate

Univariate sensitivity analysis based on the original cost assumptions was performed using identical parameter ranges to those used in the written submission.

Figure 3: All RVO (Figure 29 of original submission)

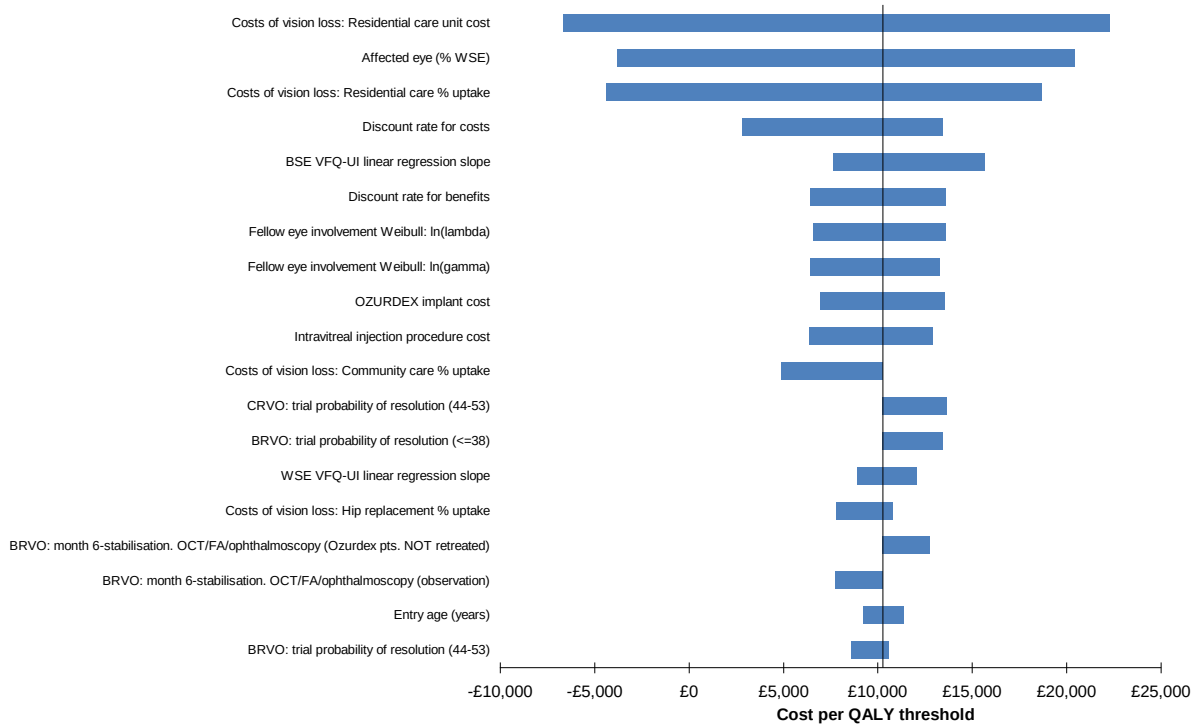


Figure 4: CRVO (Figure 30 of original submission)

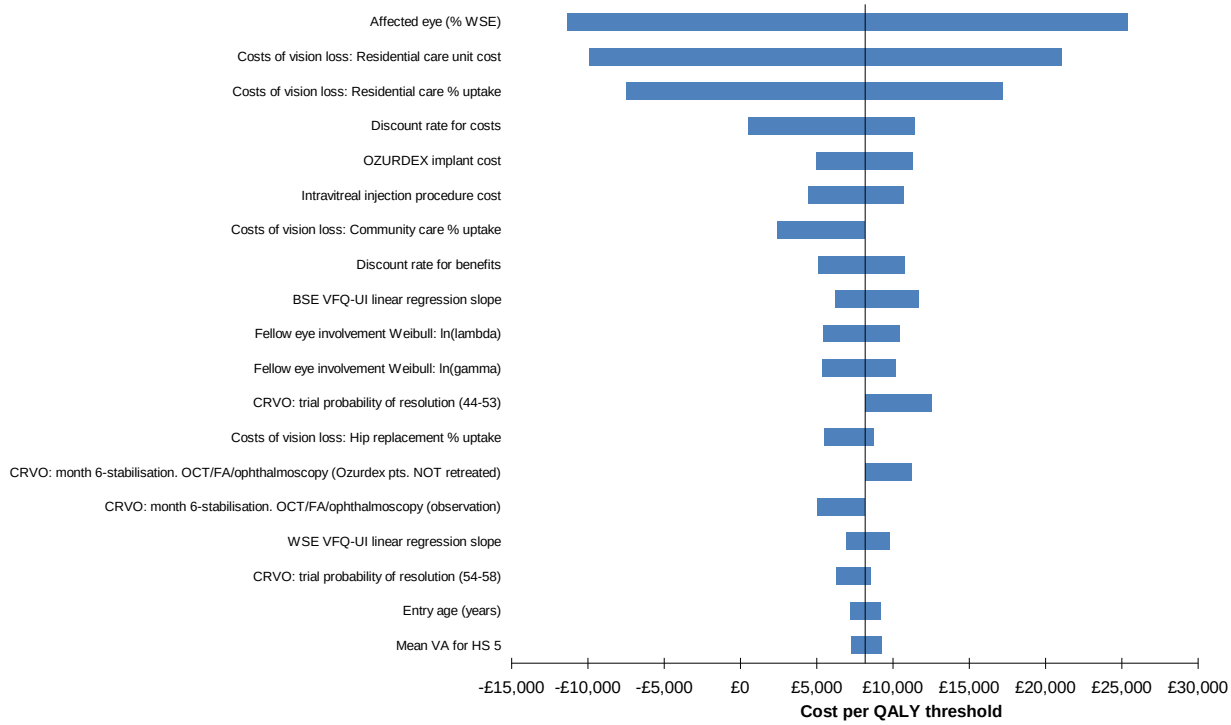


Figure 5: BRVO-macular haemorrhage (Figure 31 of original submission)

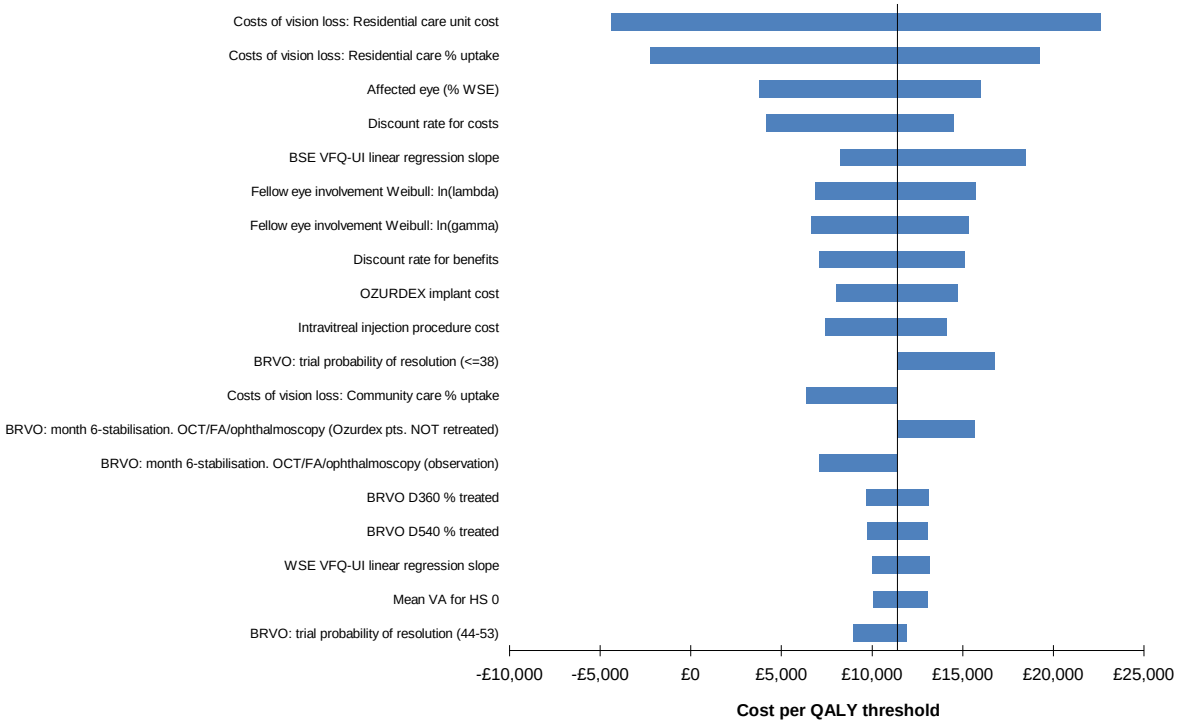
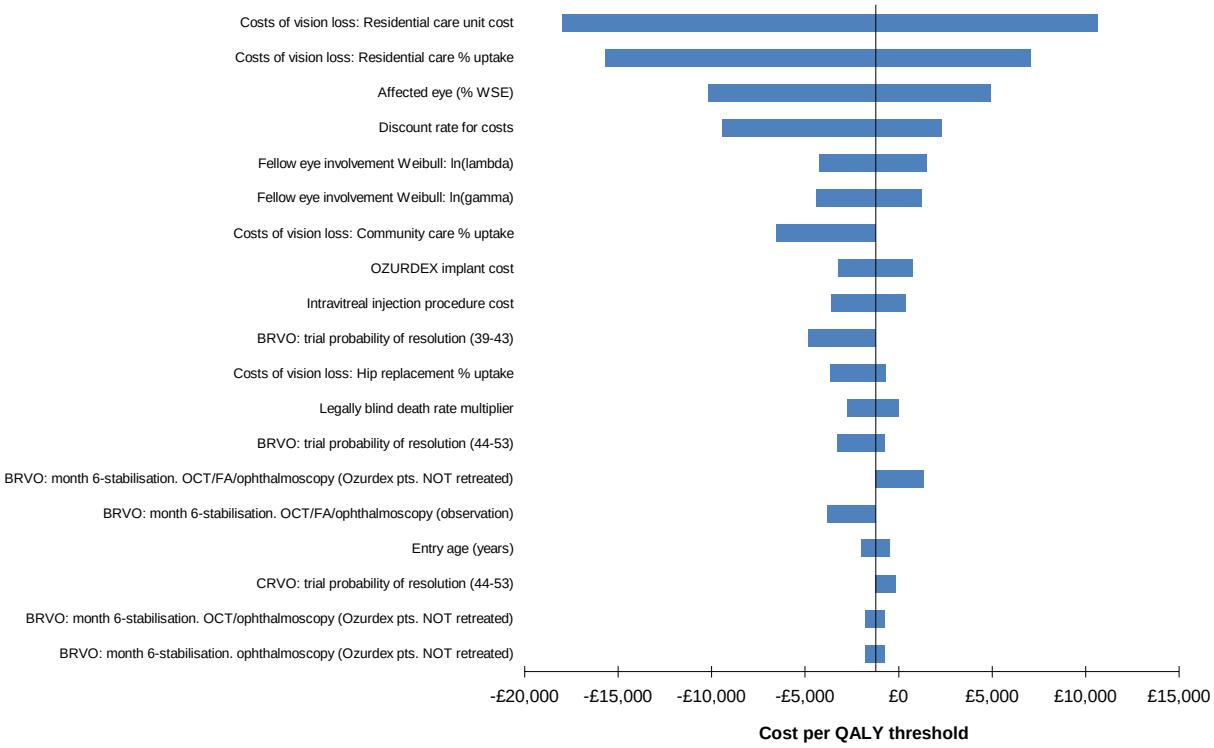


Figure 6: BRVO with previous laser (Figure 32 of original submission)



Scenario

Table 12: All RVO (Table 140 of original submission)

Scenario	Costs	QALYs	ICER
Source of utility estimates/100% BSE patients	-£10,826	0.55	Dominant
Costs of vision loss: High/High	-£9,339	0.21	Dominant
Costs of vision loss: Low/Low	£5,538	0.21	£26,295
Stabilisation of visual acuity at day 360	£1,512	0.11	£13,360
Not treated extrapolation assumptions	£3,528	0.12	£28,527
Excess mortality of blindness	£1,566	0.16	£9,529
Fellow eye occurrence	£1,734	0.26	£6,761
Discounting	£2,834	0.29	£9,706
Constant trial proportion retreated	£5,350	0.23	£23,077
All patients start in ETDRS 39-43 letters	£983	0.24	£4,116
Visual decline of 1.5% per 6 months	£2,135	0.20	£10,764
84% FEO results in ME	£2,406	0.20	£12,052

Table 13: CRVO (Table 141 of original submission)

Scenario	Costs	QALYs	ICER
Source of utility estimates/100% BSE patients	-£26,788	0.81	Dominant
Costs of vision loss: High/High	-£14,379	0.29	Dominant
Costs of vision loss: Low/Low	£7,243	0.29	£25,290
Stabilisation of visual acuity at day 360	£836	0.14	£6,064
Not treated extrapolation assumptions	£4,320	0.20	£22,009
Excess mortality of blindness	£1,500	0.22	£6,753
Fellow eye occurrence	£1,970	0.33	£6,029
Discounting	£3,279	0.40	£8,295
Constant trial proportion retreated	£4,774	0.34	£13,969
All patients start in ETDRS 39-43 letters	£1,356	0.30	£4,576
Visual decline of 1.5% per 6 months	£2,354	0.27	£8,731
84% FEO results in ME	£2,603	0.28	£9,403

Table 14: BRVO – macular haemorrhage (Table 142 of original submission)

Scenario	Costs	QALYs	ICER
Source of utility estimates/100% BSE patients	-£2,729	0.43	Dominant
Costs of vision loss: High/High	-£6,944	0.18	Dominant
Costs of vision loss: Low/Low	£4,630	0.18	£26,338
Stabilisation of visual acuity at day 360	£1,831	0.11	£17,236
Not treated extrapolation assumptions	£3,061	0.09	£33,879
Excess mortality of blindness	£1,525	0.14	£11,033
Fellow eye occurrence	£1,523	0.23	£6,756
Discounting	£2,547	0.24	£10,422
Constant trial proportion retreated	£5,653	0.18	£31,255
All patients start in ETDRS 39-43 letters	£913	0.20	£4,660
Visual decline of 1.5% per 6 months	£1,950	0.17	£11,758
84% FEO results in ME	£2,242	0.16	£13,679

Table 15: BRVO with previous laser (Table 143 of original submission)

Scenario	Costs	QALYs	ICER
Source of utility estimates/100% BSE patients	-£14,735	0.75	Dominant
Costs of vision loss: High/High	-£16,133	0.29	Dominant
Costs of vision loss: Low/Low	£4,267	0.29	£14,614
Stabilisation of visual acuity at day 360	£620	0.19	£3,253
Not treated extrapolation assumptions	£799	0.18	£4,364
Excess mortality of blindness	-£1,200	0.23	Dominant
Fellow eye occurrence	-£1,476	0.36	Dominant
Discounting	£685	0.40	£1,695
Constant trial proportion retreated	£1,745	0.38	£4,592
All patients start in ETDRS 39-43 letters	-£4,232	0.43	Dominant
Visual decline of 1.5% per 6 months	-£414	0.28	Dominant
84% FEO results in ME	£63	0.28	£230

Probabilistic

Scatter plots

The results of probabilistic analysis using the original cost assumptions were based on 5,000 Monte Carlo Simulations for each patient population using identical distributions to those in the original submission. 5,000 simulations were considered adequate on the grounds that after this number of simulations the results appear to be stable based on the average net monetary benefit (Figure 7).

Figure 7: Average net monetary benefit over simulations with λ=simulation average ICER (i.e. NMB=£0 on average)

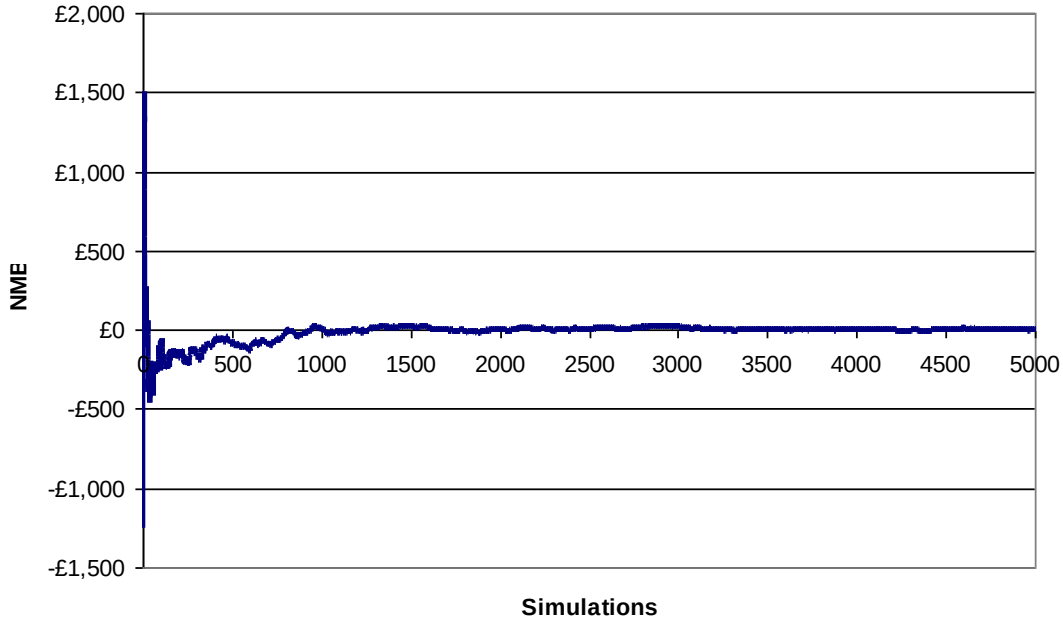


Figure 8: All RVO. Mean ICER is £10,109 (Figure 33 of original submission)

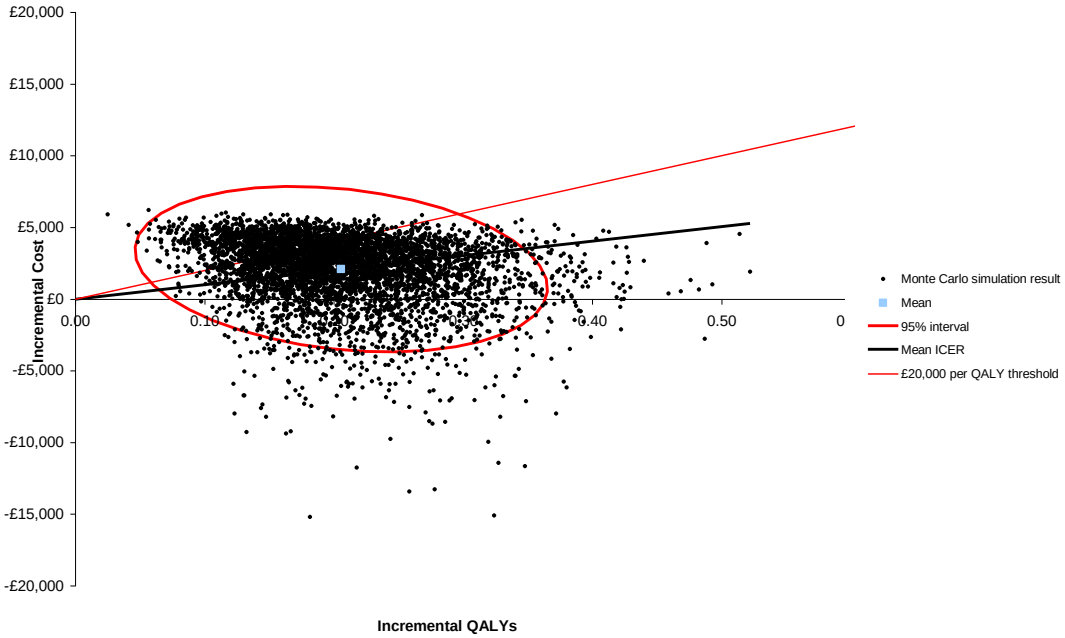


Figure 9: CRVO. Mean ICER is £8,370 (Figure 34 of original submission)

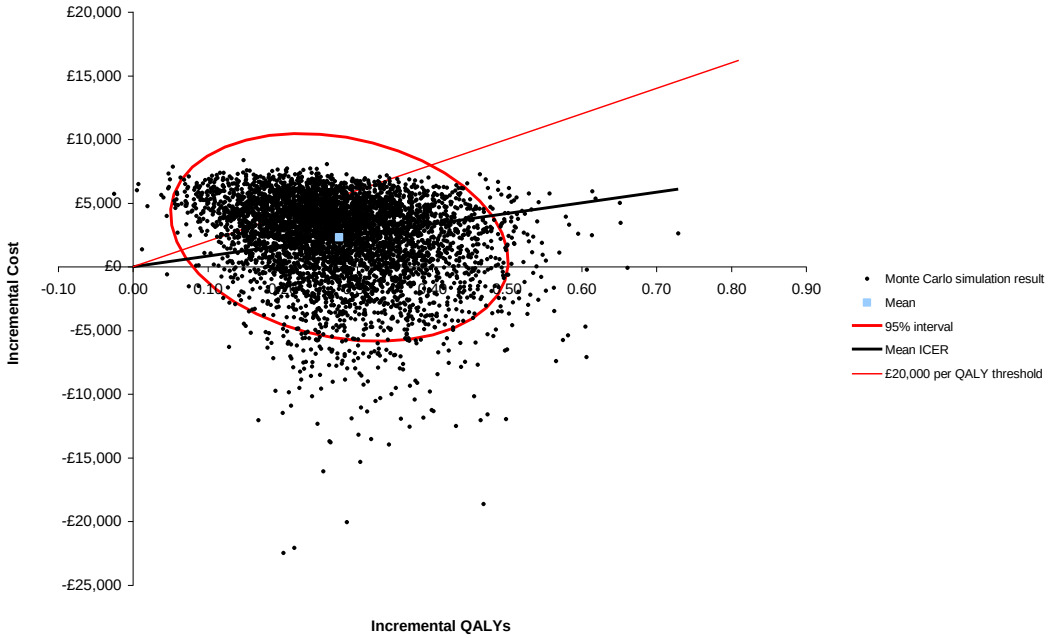


Figure 10: BRVO-macular haemorrhage. Mean ICER is £11,298 (Figure 35 of original submission)

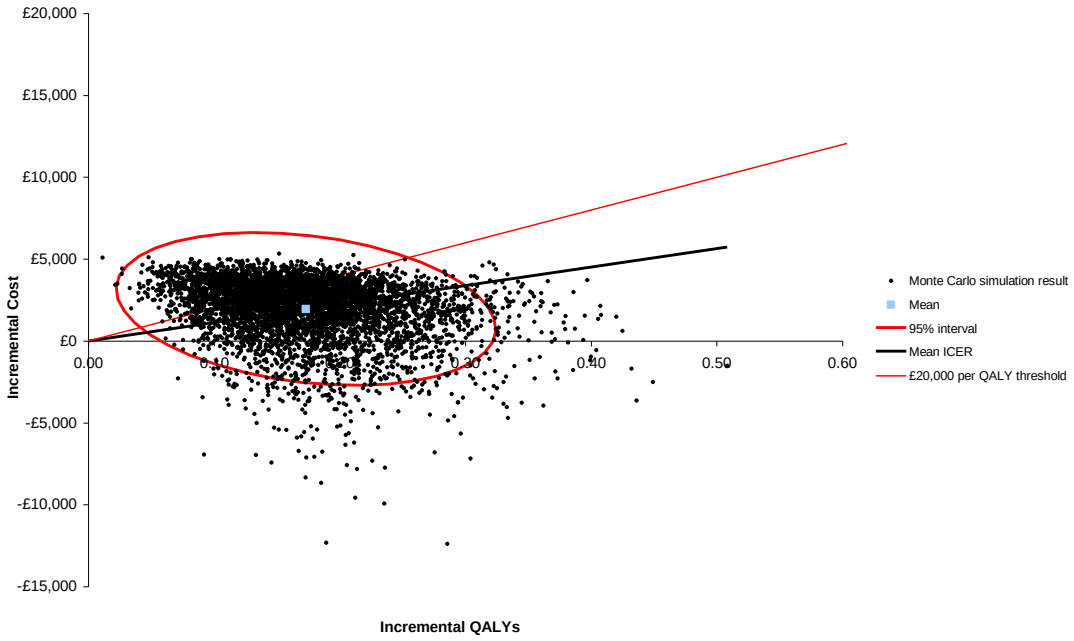
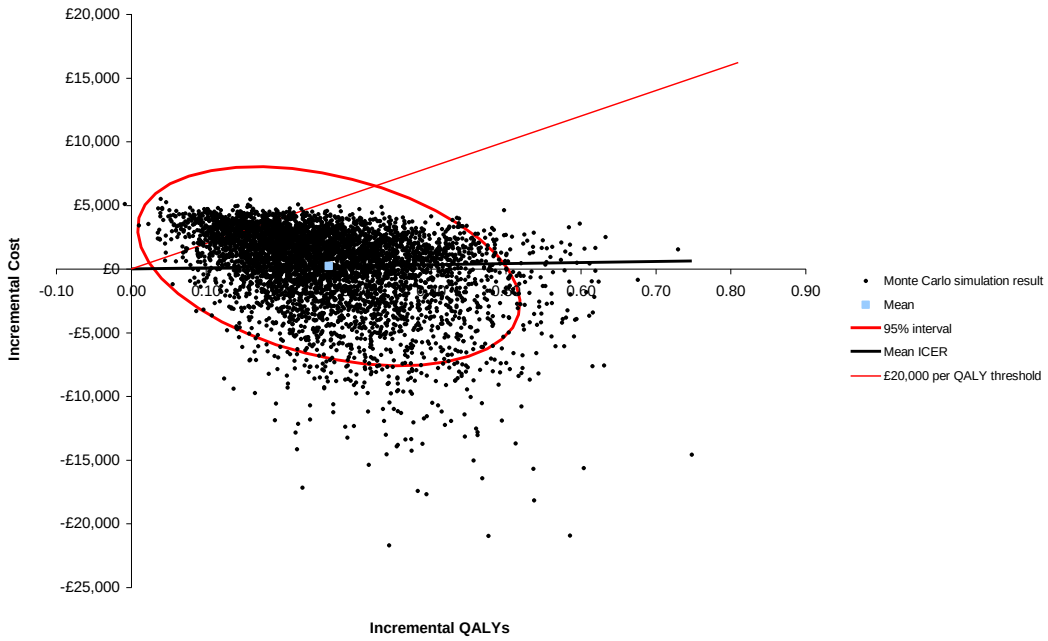


Figure 11: BRVO with previous laser. Mean ICER is £836 (Figure 36 of original submission)



Cost-effectiveness acceptability curves (CEACs)

Figure 12: All RVO. Probability cost-effective at £20,000 per QALY is 75% (Figure 37 of original submission)

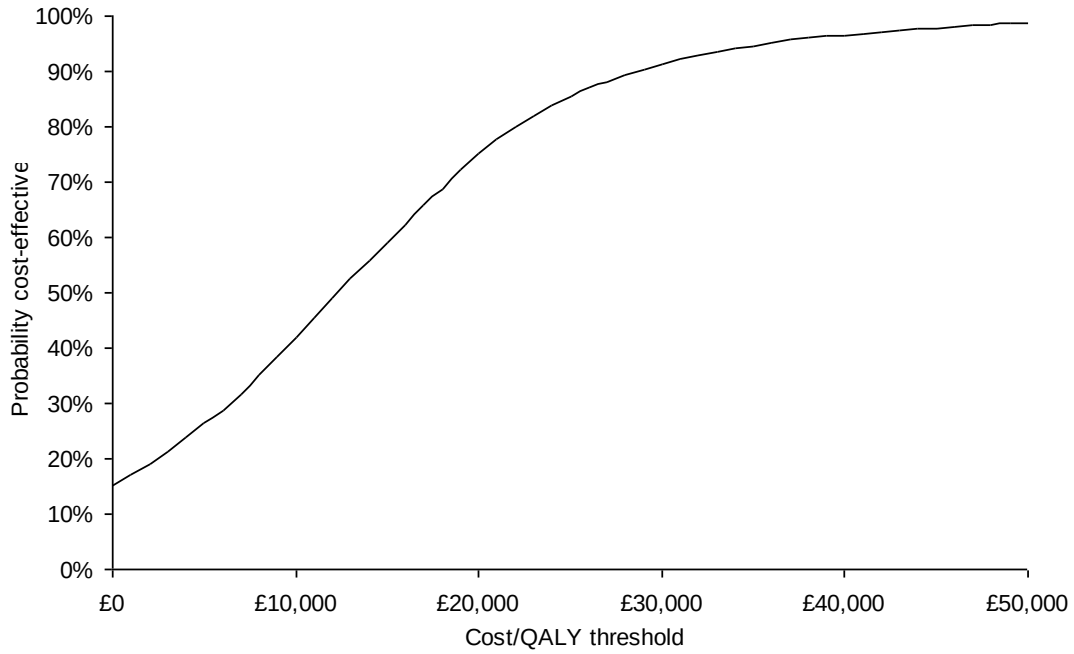


Figure 13: CRVO. Probability cost-effective at £20,000 per QALY is 78% (Figure 38 of original submission)

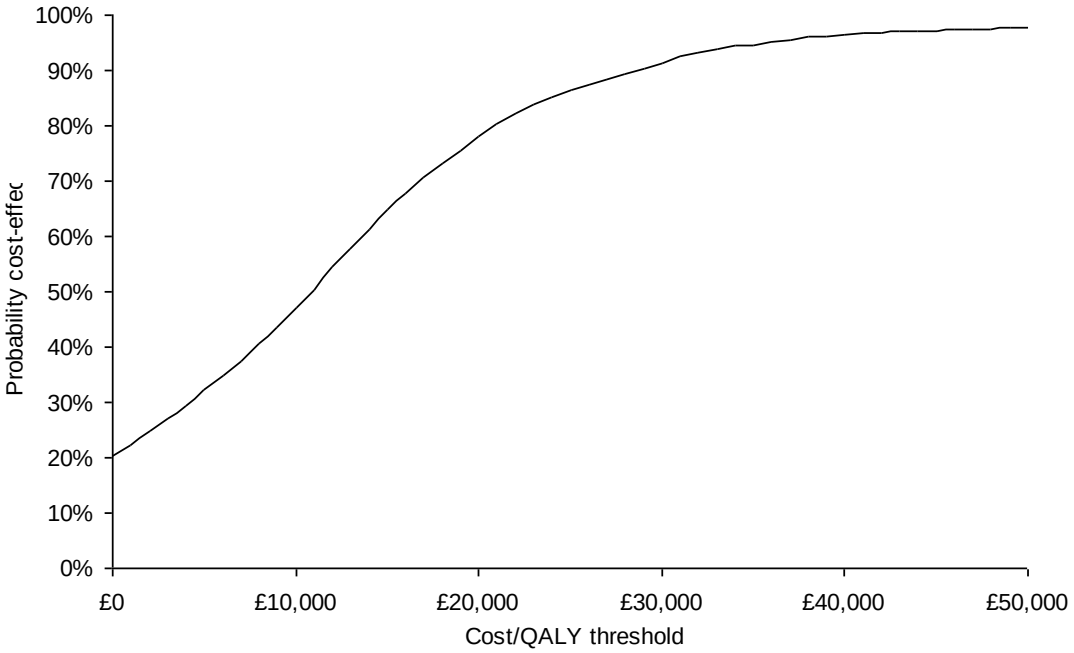


Figure 14: BRVO-macular haemorrhage. Probability cost-effective at £20,000 per QALY is 71% (Figure 39 of original submission)

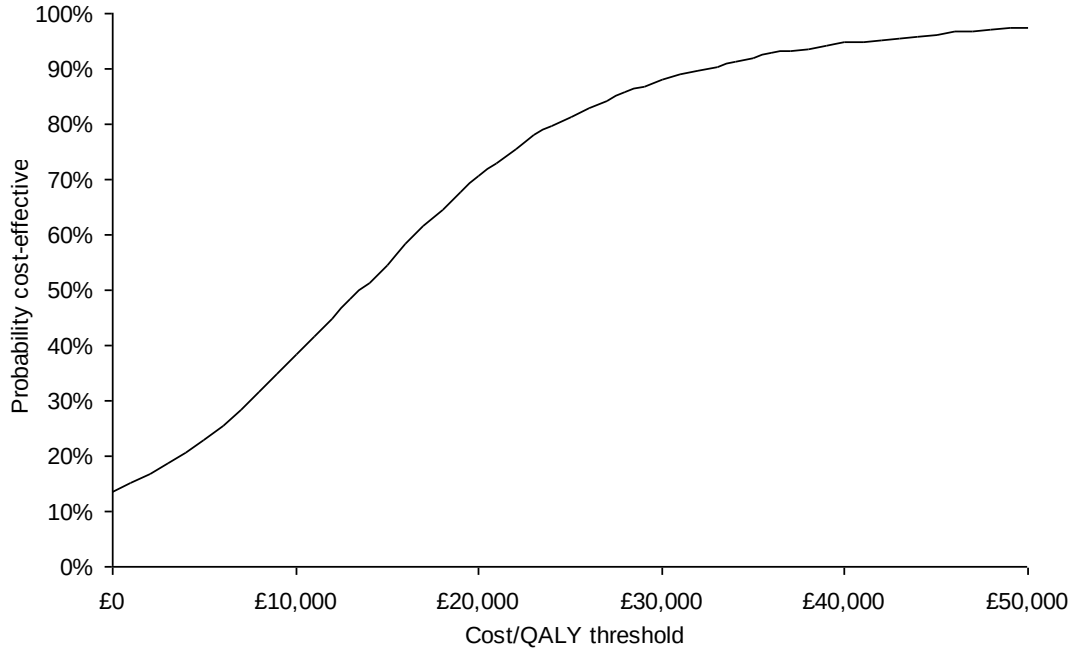
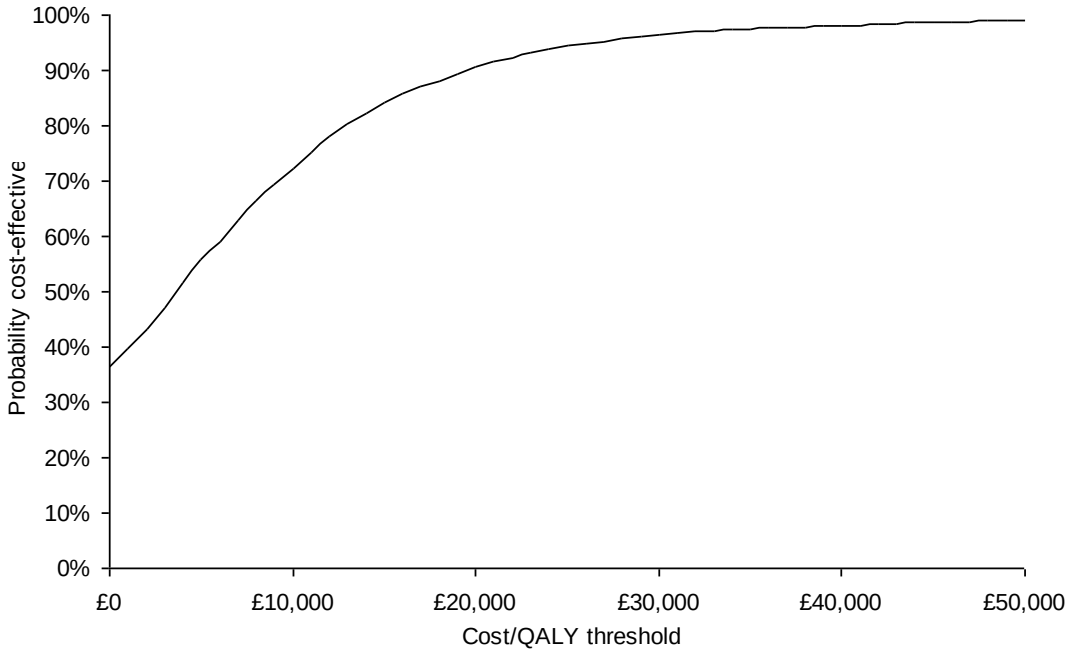


Figure 15: BRVO with previous laser therapy. Probability cost-effective at £20,000 per QALY is 91% (Figure 40 of original submission)



Sensitivity analysis: Revised cost assumptions

Deterministic

Univariate

Univariate sensitivity analysis based on the revised cost assumptions was performed using identical parameter ranges to those used in the written submission with the exception of the three cost parameters identified for revision in the ERG draft report. Table 16 details the revised parameters and the ranges used in sensitivity analyses.

Table 16: Revised parameter values and ranges used in sensitivity analysis

Variable	Default value	Reference	Lower value	Upper value	Reference for Uncertainty	Distribution in PSA	S.E.	n	Alpha	Beta
Intravitreal injection procedure cost	£150	Updated based on draft ERG report	£90	£184	Lower/upper quartile of unit cost. SE is approximation based on IQR.	Lognormal	0.05	95		
Cataract cost	£789	Updated based on draft ERG report	£636	£923	Lower/upper quartile unit cost (weighted by activity). SE is approximation based on IQR.	Lognormal	0.02	162		
Costs of vision loss: Residential care unit cost	£16,999	Updated based on draft ERG report	£4,805	£33,597	Upper: Annual cost for local authority residential care. Lower: Annual cost for local authority sheltered housing for older people (housing costs only). Both are multiplied by 0.7.	Gamma	6426.75		7	2430

Figure 16: All RVO (Figure 29 of original submission)

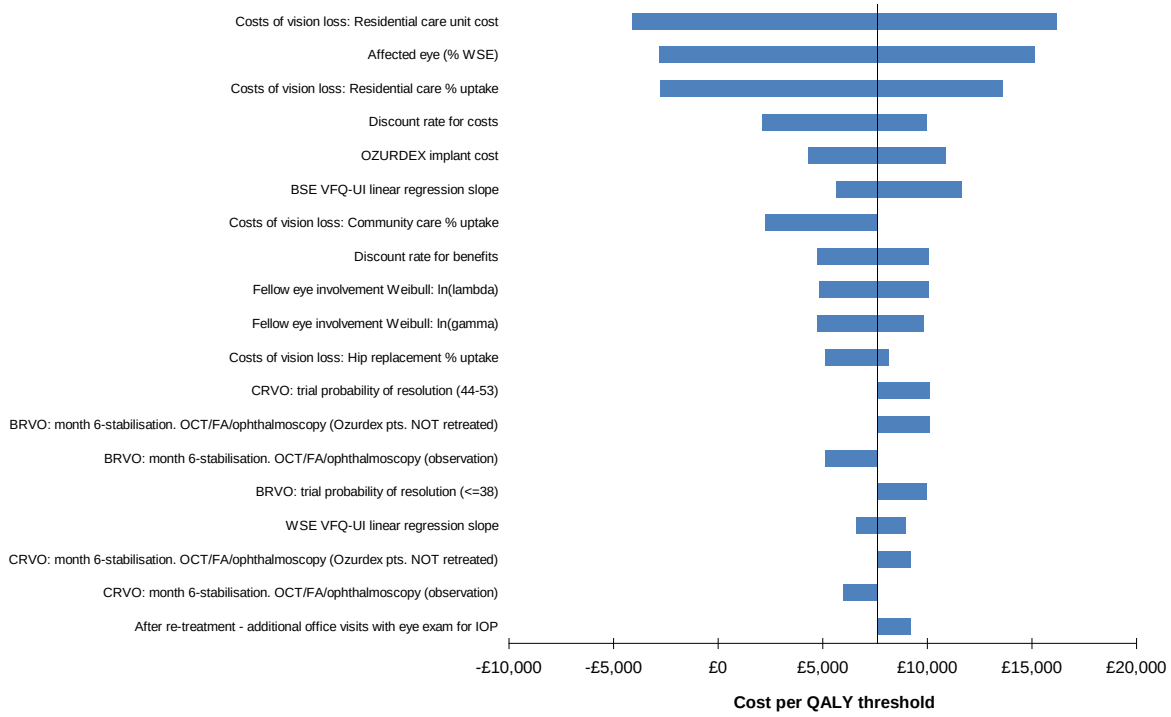


Table 17: CRVO (Figure 30 of original submission)

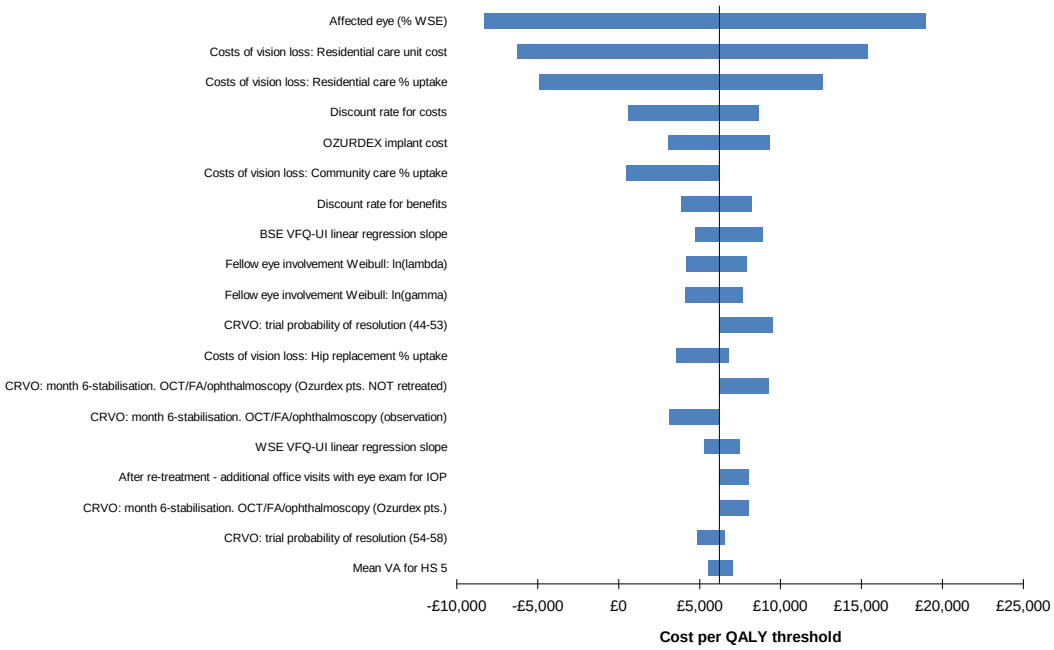


Figure 17: BRVO-macular haemorrhage (Figure 31 of original submission)

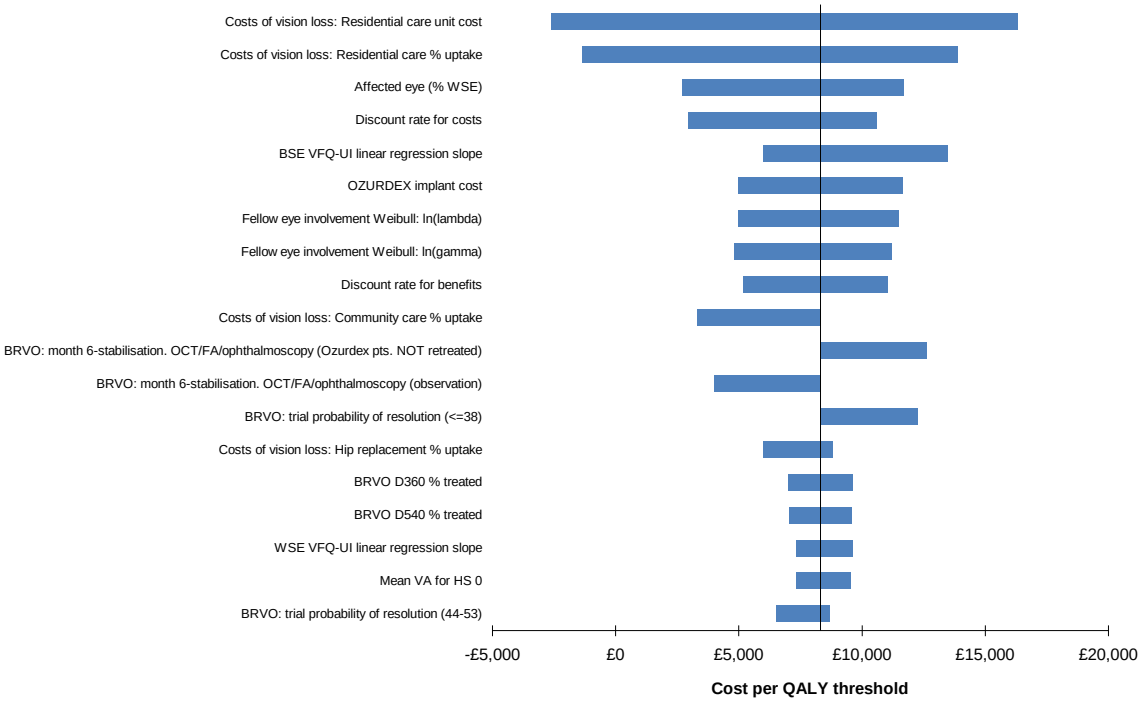
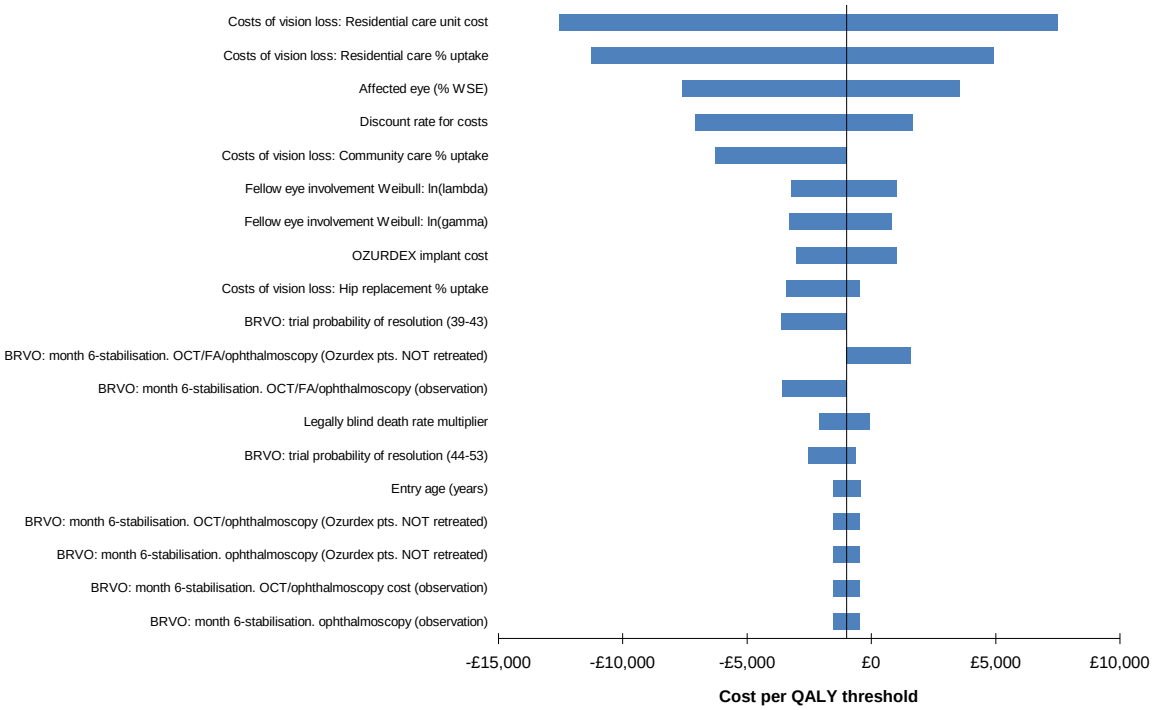


Figure 18: BRVO with previous laser (Figure 32 of original submission)



Scenario

Table 18: All RVO (Table 140 of original submission)

Scenario	Costs	QALYs	ICER
Source of utility estimates/100% BSE patients	-£8,010	0.55	Dominant
Costs of vision loss: High/High	-£10,933	0.21	Dominant
Costs of vision loss: Low/Low	£3,944	0.21	£18,725
Stabilisation of visual acuity at day 360	£1,068	0.11	£9,436
Not treated extrapolation assumptions	£2,614	0.12	£21,139
Excess mortality of blindness	£1,162	0.16	£7,070
Fellow eye occurrence	£1,288	0.26	£5,022
Discounting	£2,099	0.29	£7,189
Constant trial proportion retreated	£4,062	0.23	£17,519
All patients start in ETDRS 39-43 letters	£730	0.24	£3,058
Visual decline of 1.5% per 6 months	£1,583	0.20	£7,981
84% FEO results in ME	£1,784	0.20	£8,937

Table 19: CRVO (Table 141 of original submission)

Scenario	Costs	QALYs	ICER
Source of utility estimates/100% BSE patients	-£19,776	0.81	Dominant
Costs of vision loss: High/High	-£16,440	0.29	Dominant
Costs of vision loss: Low/Low	£5,182	0.29	£18,094
Stabilisation of visual acuity at day 360	£569	0.14	£4,129
Not treated extrapolation assumptions	£3,248	0.20	£16,551
Excess mortality of blindness	£1,161	0.22	£5,226
Fellow eye occurrence	£1,512	0.33	£4,628
Discounting	£2,475	0.40	£6,260
Constant trial proportion retreated	£3,667	0.34	£10,731
All patients start in ETDRS 39-43 letters	£1,055	0.30	£3,558
Visual decline of 1.5% per 6 months	£1,793	0.27	£6,651
84% FEO results in ME	£1,979	0.28	£7,147

Table 20: BRVO-macular haemorrhage (Table 142 of original submission)

Scenario	Costs	QALYs	ICER
Source of utility estimates/100% BSE patients	-£2,042	0.43	Dominant
Costs of vision loss: High/High	-£8,292	0.18	Dominant
Costs of vision loss: Low/Low	£3,282	0.18	£18,667
Stabilisation of visual acuity at day 360	£1,303	0.11	£12,267
Not treated extrapolation assumptions	£2,243	0.09	£24,830
Excess mortality of blindness	£1,106	0.14	£8,004
Fellow eye occurrence	£1,106	0.23	£4,906
Discounting	£1,862	0.24	£7,619
Constant trial proportion retreated	£4,269	0.18	£23,604
All patients start in ETDRS 39-43 letters	£654	0.20	£3,334
Visual decline of 1.5% per 6 months	£1,421	0.17	£8,568
84% FEO results in ME	£1,637	0.16	£9,989

Table 21: BRVO with previous laser (Table 143 of original submission)

Scenario	Costs	QALYs	ICER
Source of utility estimates/100% BSE patients	-£10,930	0.75	Dominant
Costs of vision loss: High/High	-£17,481	0.29	Dominant
Costs of vision loss: Low/Low	£2,919	0.29	£9,996
Stabilisation of visual acuity at day 360	£406	0.19	£2,133
Not treated extrapolation assumptions	£569	0.18	£3,107
Excess mortality of blindness	-£911	0.23	Dominant
Fellow eye occurrence	-£1,114	0.36	Dominant
Discounting	£484	0.40	£1,197
Constant trial proportion retreated	£1,376	0.38	£3,621
All patients start in ETDRS 39-43 letters	-£3,156	0.43	Dominant
Visual decline of 1.5% per 6 months	-£329	0.28	Dominant
84% FEO results in ME	£24	0.28	£89

Probabilistic

Scatter plots

The results of probabilistic analysis using the revised cost assumptions were based on 5,000 Monte Carlo Simulations for each patient population using identical distributions to those in the original submission with the exception of the three revised cost parameters which are detailed in Table 16.

Figure 19: All RVO. Mean ICER is £7,494 (Figure 33 of original submission)

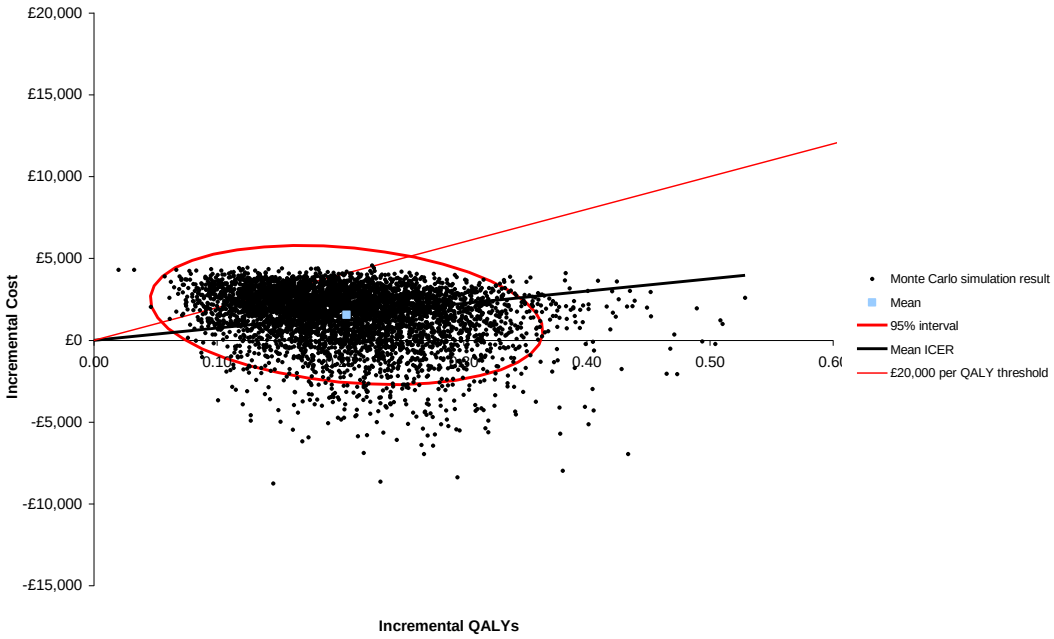


Figure 20: CRVO. Mean ICER is £6,522 (Figure 34 of original submission)

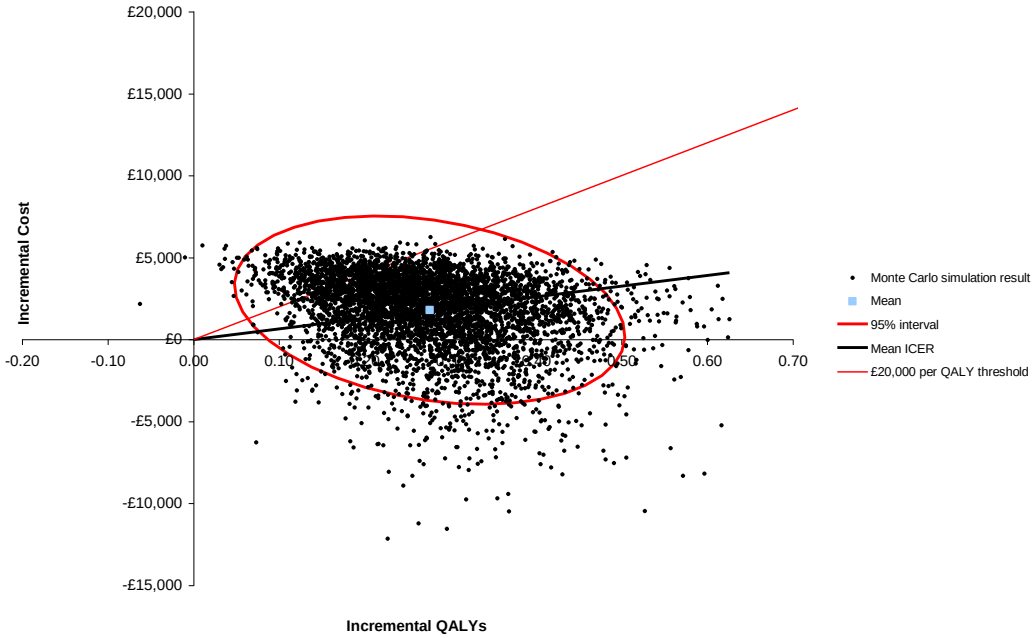


Figure 21: BRVO-with macular haemorrhage. Mean ICER is £8,183 (Figure 35 of original submission)

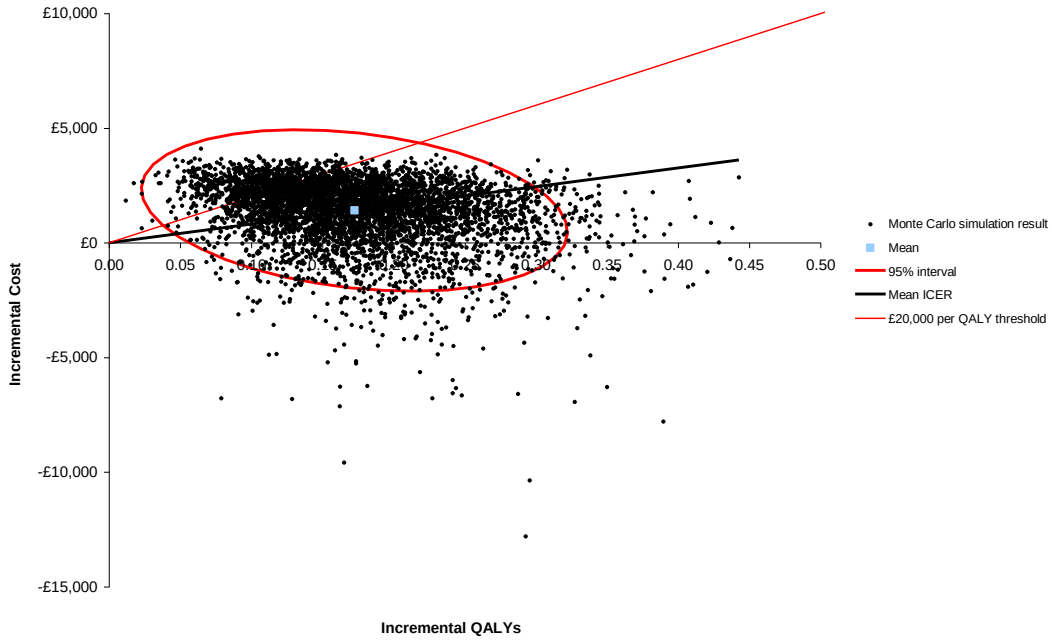
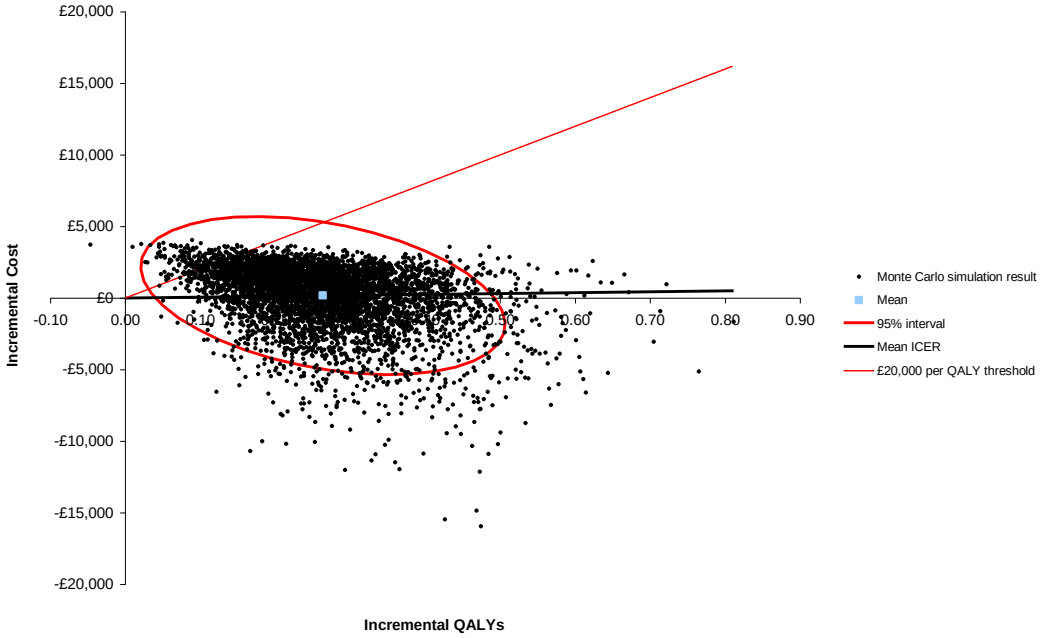


Figure 22: BRVO with previous laser. Mean ICER is £631 (Figure 36 of original submission)



Cost-effectiveness acceptability curves (CEACs)

Figure 23: All RVO. Probability cost-effective at £20,000 per QALY is 88% (Figure 37 of original submission)

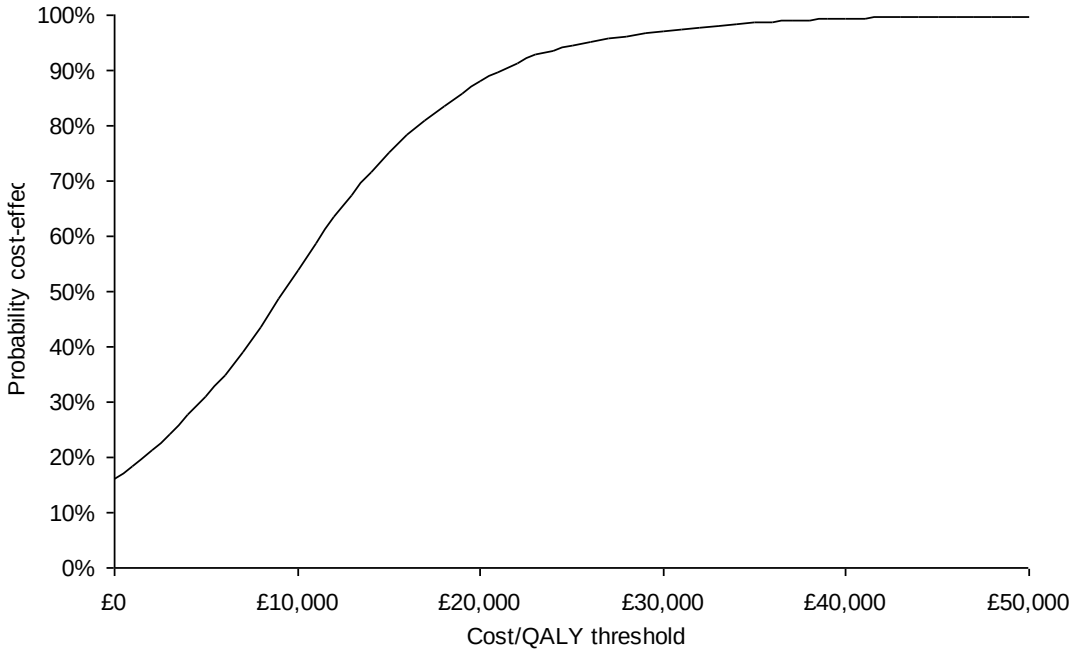


Figure 24: CRVO. Probability cost-effective at £20,000 per QALY is 88% (Figure 38 of original submission)

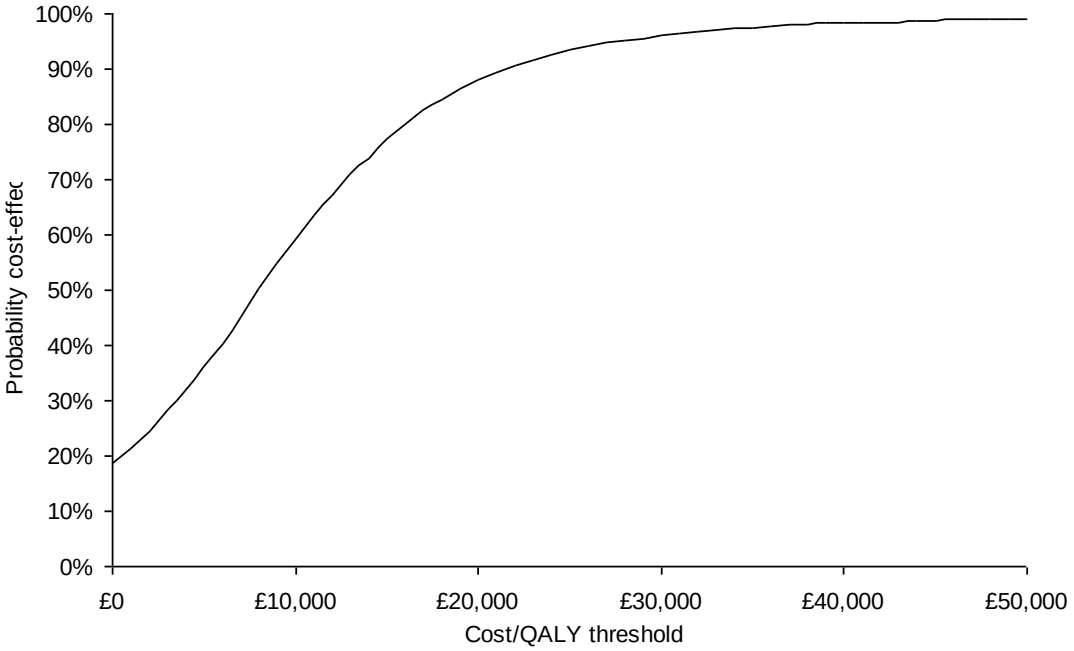


Figure 25: BRVO-macular haemorrhage. Probability cost-effective at £20,000 per QALY is 85% (Figure 39 of original submission)

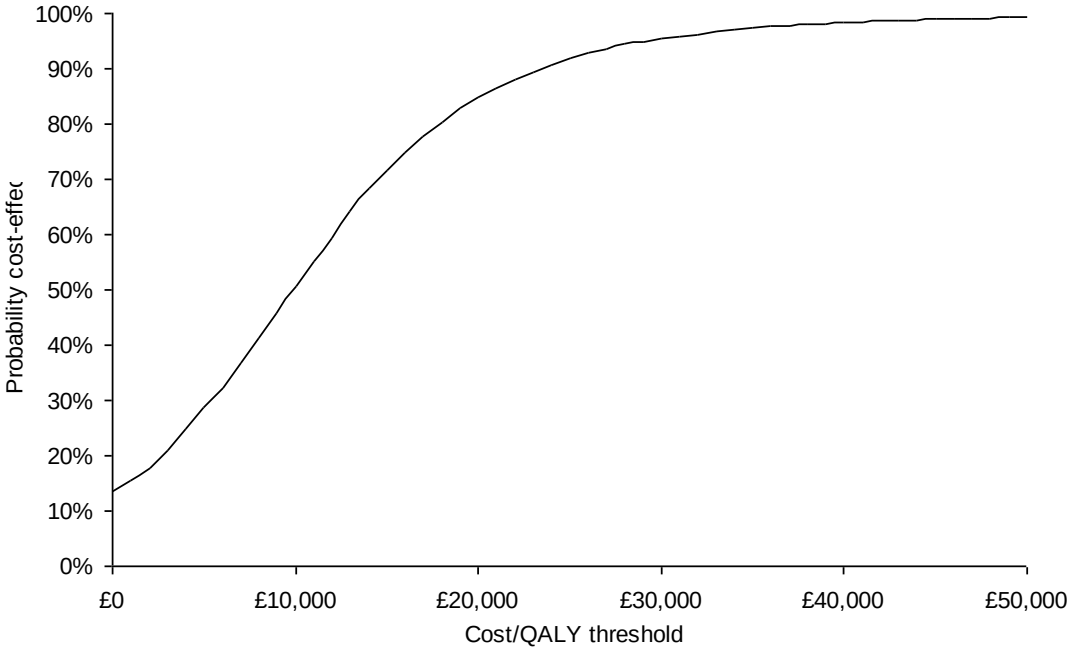
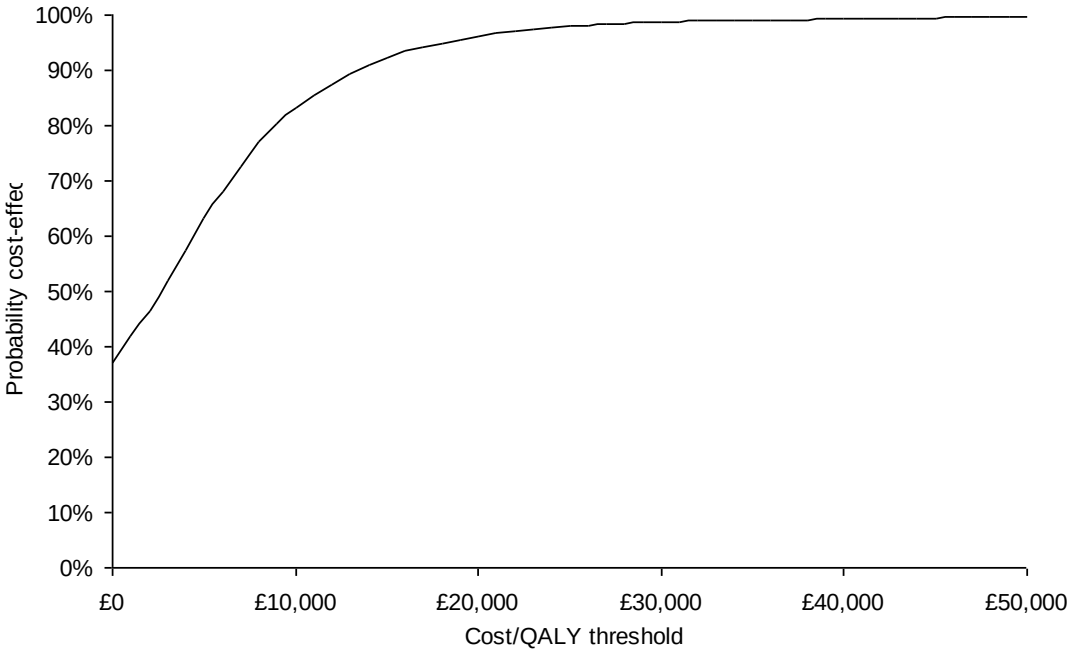


Figure 26: BRVO with previous laser. Probability cost-effective at £20,000 per QALY is 96% (Figure 40 of original submission)



Appendix A: Disaggregated model results (based on original cost assumptions)

Table 22: Comparison of trial and model outcomes in treated patients with CRVO

Health state	Baseline		Day 180		Day 360	
	GENEVA 008&009 result	Model result	GENEVA 008&009 result	Model result	GENEVA 008&009 result	Model result
>=69	0.0%	0.4%	20.3%	20.8%	20.2%	20.9%
59-68	35.3%	36.4%	19.5%	19.9%	24.6%	19.0%
54-58	18.0%	21.1%	14.3%	14.3%	13.2%	9.2%
44-53	18.0%	16.4%	17.3%	17.2%	21.9%	22.2%
39-43	12.0%	8.9%	6.0%	5.9%	3.5%	2.0%
<=38	16.5%	16.8%	22.6%	21.9%	16.7%	26.7%

Table 23: Comparison of trial and model outcomes in treated patients with BRVO-macular haemorrhage

Health state	Baseline		Day 180		Day 360	
	GENEVA 008&009 result	Model result	GENEVA 008&009 result	Model result	GENEVA 008&009 result	Model result
>=69	0.0%	0.6%	36.5%	36.7%	38.6%	40.6%
59-68	42.0%	41.2%	30.2%	30.3%	21.8%	28.9%
54-58	16.9%	18.6%	10.2%	10.2%	13.4%	8.2%
44-53	25.1%	23.7%	12.5%	12.5%	14.9%	11.0%
39-43	6.7%	7.6%	4.7%	4.6%	4.5%	3.5%
<=38	9.4%	8.3%	5.9%	5.7%	6.9%	7.8%

Table 24: Comparison of trial and model outcomes in treated patients with BRVO with previous laser

Health state	Baseline		Day 180		Day 360	
	GENEVA 008&009 result	Model result	GENEVA 008&009 result	Model result	GENEVA 008&009 result	Model result
>=69	0.0%	0.0%	22.2%	23.6%	22.6%	24.1%
59-68	27.8%	31.9%	36.1%	37.3%	22.6%	32.7%
54-58	19.4%	22.2%	11.1%	10.9%	16.1%	14.4%
44-53	27.8%	25.0%	11.1%	10.7%	22.6%	7.6%
39-43	16.7%	13.9%	5.6%	5.3%	6.5%	5.4%
<=38	8.3%	6.9%	13.9%	12.2%	9.7%	15.9%

Table 25: Comparison of trial and model outcomes in observation patients with CRVO

Health state	Baseline		Day 180	
	GENEVA 008&009 result	Model result	GENEVA 008&009 result	Model result
>=69	0.68%	0.36%	23.81%	23.22%
59-68	37.41%	36.43%	17.01%	16.76%
54-58	23.81%	21.07%	10.20%	10.16%
44-53	14.97%	16.43%	15.65%	15.80%
39-43	6.12%	8.93%	4.76%	4.87%
<=38	17.01%	16.79%	28.57%	29.19%

Table 26: Comparison of trial and model outcomes in observation patients with BRVO-macular haemorrhage

Health state	Baseline		Day 180	
	GENEVA 008&009 result	Model result	GENEVA 008&009 result	Model result
>=69	1.15%	0.58%	29.62%	29.28%
59-68	40.38%	41.17%	30.00%	29.86%
54-58	20.38%	18.64%	11.54%	11.58%
44-53	22.31%	23.69%	14.62%	14.74%
39-43	8.46%	7.57%	5.00%	5.09%
<=38	7.31%	8.35%	9.23%	9.45%

Table 27: Comparison of trial and model outcomes in observation patients with BRVO with previous laser

Health state	Baseline		Day 180	
	GENEVA 008&009 result	Model result	GENEVA 008&009 result	Model result
>=69	0.00%	0.00%	13.89%	12.89%
59-68	36.11%	31.94%	30.56%	28.70%
54-58	25.00%	22.22%	22.22%	21.91%
44-53	22.22%	25.00%	11.11%	11.02%
39-43	11.11%	13.89%	11.11%	12.28%
<=38	5.56%	6.94%	11.11%	13.22%

Table 28: Life years and QALYs by health state in patients with RVO

Treated eye	Health state	Ozurdex		Observation	
		LYs	QALYs	LYs	QALYs
WSE	>=69	3.97	3.42	2.65	2.29
	59-68	2.63	2.23	2.36	2.01
	54-58	0.80	0.67	0.82	0.69
	44-53	1.52	1.26	1.20	1.00
	39-43	0.29	0.24	0.50	0.41
	<=38	1.17	0.96	2.84	2.31
BSE	>=69	1.34	1.03	0.89	0.69
	59-68	0.89	0.64	0.80	0.57
	54-58	0.27	0.19	0.28	0.19
	44-53	0.51	0.34	0.40	0.27
	39-43	0.10	0.06	0.17	0.11
	<=38	0.35	0.21	0.84	0.50

Table 29: Life years and QALYs by health state in patients with CRVO

Treated eye	Health state	Ozurdex		Observation	
		LYs	QALYs	LYs	QALYs
WSE	>=69	2.81	2.43	2.04	1.76
	59-68	2.57	2.18	1.11	0.94
	54-58	0.80	0.67	0.56	0.47
	44-53	2.39	1.99	1.06	0.88
	39-43	0.19	0.15	0.45	0.37
	<=38	1.62	1.32	5.14	4.19
BSE	>=69	1.18	0.91	0.81	0.62
	59-68	0.88	0.63	0.63	0.45
	54-58	0.27	0.19	0.24	0.17
	44-53	0.63	0.42	0.38	0.25
	39-43	0.08	0.05	0.16	0.10
	<=38	0.40	0.24	1.11	0.67

Table 30: Life years and QALYs by health state in patients with BRVO-macular haemorrhage

Treated eye	Health state	Ozurdex		Observation	
		LYs	QALYs	LYs	QALYs
WSE	>=69	4.75	4.10	3.13	2.70
	59-68	2.42	2.06	2.74	2.32
	54-58	0.79	0.67	0.95	0.80
	44-53	1.05	0.87	1.30	1.08
	39-43	0.36	0.29	0.55	0.45
	<=38	1.00	0.81	1.71	1.39
BSE	>=69	1.47	1.13	0.98	0.75
	59-68	0.83	0.60	0.81	0.58
	54-58	0.27	0.18	0.29	0.20
	44-53	0.45	0.30	0.42	0.28
	39-43	0.11	0.07	0.18	0.11
	<=38	0.33	0.20	0.71	0.43

Table 31: Life years and QALYs by health state in patients with BRVO with previous laser

Treated eye	Health state	Ozurdex		Observation	
		LYs	QALYs	LYs	QALYs
WSE	>=69	2.72	2.34	0.73	0.63
	59-68	2.51	2.13	2.01	1.71
	54-58	1.68	1.41	1.99	1.67
	44-53	0.98	0.82	0.89	0.75
	39-43	0.53	0.44	0.84	0.69
	<=38	1.96	1.60	3.91	3.19
BSE	>=69	0.92	0.70	0.33	0.26
	59-68	0.85	0.61	0.61	0.44
	54-58	0.50	0.35	0.57	0.39
	44-53	0.43	0.29	0.31	0.21
	39-43	0.16	0.10	0.25	0.16
	<=38	0.56	0.34	1.23	0.74

Table 32: Disaggregated QALYs – all RVO

Treated eye	Health state	QALY Observation	QALY Ozurdex	Increment	Absolute increment	% absolute increment
WSE	>=69	2.29	3.42	1.14	1.14	49.7%
	59-68	2.01	2.23	0.22	0.22	11.1%
	54-58	0.69	0.67	-0.01	0.01	2.1%
	44-53	1.00	1.26	0.26	0.26	26.0%
	39-43	0.41	0.24	-0.17	0.17	42.4%
	<=38	2.31	0.96	-1.36	1.36	58.6%
BSE	>=69	0.69	1.03	0.34	0.34	50.0%
	59-68	0.57	0.64	0.06	0.06	11.3%
	54-58	0.19	0.19	0.00	0.00	2.0%
	44-53	0.27	0.34	0.07	0.07	26.4%
	39-43	0.11	0.06	-0.05	0.05	42.5%
	<=38	0.50	0.21	-0.29	0.29	58.4%

Table 33: Disaggregated QALYs - CRVO

Treated eye	Health state	QALY Observation	QALY Ozurdex	Increment	Absolute increment	% absolute increment
WSE	>=69	1.76	2.43	0.66	0.66	37.7%
	59-68	0.94	2.18	1.24	1.24	130.9%
	54-58	0.47	0.67	0.20	0.20	41.5%
	44-53	0.88	1.99	1.11	1.11	125.4%
	39-43	0.37	0.15	-0.22	0.22	59.0%
	<=38	4.19	1.32	-2.87	2.87	68.6%
BSE	>=69	0.62	0.91	0.29	0.29	46.1%
	59-68	0.45	0.63	0.18	0.18	40.1%
	54-58	0.17	0.19	0.02	0.02	11.8%
	44-53	0.25	0.42	0.16	0.16	64.0%
	39-43	0.10	0.05	-0.05	0.05	48.9%
	<=38	0.67	0.24	-0.43	0.43	64.0%

Table 34: Disaggregated QALYs - BRVO- macular haemorrhage

Treated eye	Health state	QALY Observation	QALY Ozurdex	Increment	Absolute increment	% absolute increment
WSE	>=69	2.70	4.10	1.40	1.40	52.0%
	59-68	2.32	2.06	-0.26	0.26	11.4%
	54-58	0.80	0.67	-0.13	0.13	16.4%
	44-53	1.08	0.87	-0.21	0.21	19.3%
	39-43	0.45	0.29	-0.16	0.16	35.3%
	<=38	1.39	0.81	-0.58	0.58	41.7%
BSE	>=69	0.75	1.13	0.38	0.38	50.2%
	59-68	0.58	0.60	0.01	0.01	2.4%
	54-58	0.20	0.18	-0.02	0.02	8.6%
	44-53	0.28	0.30	0.02	0.02	6.3%
	39-43	0.11	0.07	-0.04	0.04	39.5%
	<=38	0.43	0.20	-0.23	0.23	53.1%

Table 35: Disaggregated QALYs - BRVO with previous laser

Treated eye	Health state	QALY Observation	QALY Ozurdex	Increment	Absolute increment	% absolute increment
WSE	>=69	0.63	2.34	1.71	1.71	270.0%
	59-68	1.71	2.13	0.43	0.43	25.0%
	54-58	1.67	1.41	-0.26	0.26	15.8%
	44-53	0.75	0.82	0.07	0.07	9.6%
	39-43	0.69	0.44	-0.25	0.25	36.5%
	<=38	3.19	1.60	-1.59	1.59	49.9%
BSE	>=69	0.26	0.70	0.45	0.45	175.9%
	59-68	0.44	0.61	0.17	0.17	38.9%
	54-58	0.39	0.35	-0.04	0.04	11.4%
	44-53	0.21	0.29	0.08	0.08	38.3%
	39-43	0.16	0.10	-0.06	0.06	38.9%
	<=38	0.74	0.34	-0.40	0.40	54.3%

Table 36: Costs by category – all RVO

Item	Cost Ozurdex	Cost Observation	Increment	Absolute increment	% absolute increment
Drug acquisition	£2,777.78	£0.00	£2,777.78	£2,777.78	-
Drug administration	£2,068.97	£0.00	£2,068.97	£2,068.97	-
Routine visits and monitoring	£3,711.52	£2,817.31	£894.20	£894.20	32%
Adverse events	£408.11	£0.00	£408.11	£408.11	-
Vision loss: Community care	£142.05	£341.20	-£199.16	£199.16	58%
Vision loss: Residential care	£2,538.13	£6,096.71	-£3,558.58	£3,558.58	58%
Vision loss: Depression	£68.55	£164.65	-£96.10	£96.10	58%
Vision loss: Hip replacement	£94.16	£226.18	-£132.02	£132.02	58%
Total	**£11,809**	**£9,646**	**£2,163**	**£2,163**	**22%**

Table 37: Costs by category - CRVO

Item	Cost Ozurdex	Cost Observation	Increment	Absolute increment	% absolute increment
Drug acquisition	£3,589.09	£0.00	£3,589.09	£3,589.09	-
Drug administration	£2,673.25	£0.00	£2,673.25	£2,673.25	-
Routine visits and monitoring	£4,470.69	£3,160.57	£1,310.12	£1,310.12	41%
Adverse events	£558.81	£0.00	£558.81	£558.81	-
Vision loss: Community care	£163.24	£452.69	-£289.45	£289.45	64%
Vision loss: Residential care	£2,916.87	£8,088.75	-£5,171.88	£5,171.88	64%
Vision loss: Depression	£78.77	£218.45	-£139.67	£139.67	64%
Vision loss: Hip replacement	£108.21	£300.08	-£191.87	£191.87	64%
Total	**£14,559**	**£12,221**	**£2,338**	**£2,338**	**19%**

Table 38: Costs by category - BRVO- macular haemorrhage

Item	Cost Ozurdex	Cost Observation	Increment	Absolute increment	% absolute increment
Drug acquisition	£2,350.62	£0.00	£2,350.62	£2,350.62	-
Drug administration	£1,750.81	£0.00	£1,750.81	£1,750.81	-
Routine visits and monitoring	£3,311.80	£2,636.56	£675.24	£675.24	26%
Adverse events	£328.77	£0.00	£328.77	£328.77	-
Vision loss: Community care	£136.32	£291.25	-£154.93	£154.93	53%
Vision loss: Residential care	£2,435.80	£5,204.17	-£2,768.37	£2,768.37	53%
Vision loss: Depression	£65.78	£140.55	-£74.76	£74.76	53%
Vision loss: Hip replacement	£90.37	£193.07	-£102.70	£102.70	53%
Total	**£10,470**	**£8,466**	**£2,005**	**£2,005**	**24%**

Table 39: Costs by category - BRVO with previous laser

Item	Cost Ozurdex	Cost Observation	Increment	Absolute increment	% absolute increment
Drug acquisition	£2,350.53	£0.00	£2,350.53	£2,350.53	-
Drug administration	£1,750.74	£0.00	£1,750.74	£1,750.74	-
Routine visits and monitoring	£3,311.58	£2,636.25	£675.33	£675.33	26%
Adverse events	£328.75	£0.00	£328.75	£328.75	-
Vision loss: Community care	£229.12	£502.21	-£273.09	£273.09	54%
Vision loss: Residential care	£4,093.99	£8,973.60	-£4,879.61	£4,879.61	54%
Vision loss: Depression	£110.56	£242.35	-£131.78	£131.78	54%
Vision loss: Hip replacement	£151.88	£332.91	-£181.03	£181.03	54%
Total	**£12,327**	**£12,687**	**-£360**	**£360**	**3%**

Appendix B: Disaggregated model results (based on revised cost assumptions)

Note that only tables reporting costs are reported here, as the accumulation of QALYs and LYs is identical to those reported in Appendix A.

Table 40: Costs by category – all RVO

Item	Cost Ozurdex	Cost Observation	Increment	Absolute increment	% absolute increment
Drug acquisition	£2,777.78	£0.00	£2,777.78	£2,777.78	-
Drug administration	£478.93	£0.00	£478.93	£478.93	-
Routine visits and monitoring	£3,711.52	£2,817.31	£894.20	£894.20	32%
Adverse events	£403.86	£0.00	£403.86	£403.86	-
Vision loss: Community care	£142.05	£341.21	-£199.16	£199.16	58%
Vision loss: Residential care	£1,799.86	£4,323.35	-£2,523.49	£2,523.49	58%
Vision loss: Depression	£68.55	£164.65	-£96.11	£96.11	58%
Vision loss: Hip replacement	£94.16	£226.18	-£132.02	£132.02	58%
Total	**£9,477**	**£7,873**	**£1,604**	**£1,604**	**20%**

Table 41: Costs by category - CRVO

Item	Cost Ozurdex	Cost Observation	Increment	Absolute increment	% absolute increment
Drug acquisition	£3,589.09	£0.00	£3,589.09	£3,589.09	-
Drug administration	£618.81	£0.00	£618.81	£618.81	-
Routine visits and monitoring	£4,470.69	£3,160.57	£1,310.12	£1,310.12	41%
Adverse events	£552.09	£0.00	£552.09	£552.09	-
Vision loss: Community care	£163.25	£452.69	-£289.45	£289.45	64%
Vision loss: Residential care	£2,068.43	£5,735.96	-£3,667.52	£3,667.52	64%
Vision loss: Depression	£78.78	£218.45	-£139.68	£139.68	64%
Vision loss: Hip replacement	£108.21	£300.09	-£191.87	£191.87	64%
Total	**£11,649**	**£9,868**	**£1,782**	**£1,782**	**18%**

Table 42: Costs by category - BRVO- macular haemorrhage

Item	Cost Ozurdex	Cost Observation	Increment	Absolute increment	% absolute increment
Drug acquisition	£2,350.62	£0.00	£2,350.62	£2,350.62	-
Drug administration	£405.28	£0.00	£405.28	£405.28	-
Routine visits and monitoring	£3,311.80	£2,636.56	£675.24	£675.24	26%
Adverse events	£325.81	£0.00	£325.81	£325.81	-
Vision loss: Community care	£136.32	£291.26	-£154.93	£154.93	53%
Vision loss: Residential care	£1,727.29	£3,690.42	-£1,963.13	£1,963.13	53%
Vision loss: Depression	£65.78	£140.55	-£74.76	£74.76	53%
Vision loss: Hip replacement	£90.37	£193.07	-£102.70	£102.70	53%
Total	**£8,413**	**£6,952**	**£1,461**	**£1,461**	**21%**

Table 43: Costs by category - BRVO with previous laser

Item	Cost Ozurdex	Cost Observation	Increment	Absolute increment	% absolute increment
Drug acquisition	£2,350.53	£0.00	£2,350.53	£2,350.53	-
Drug administration	£405.26	£0.00	£405.26	£405.26	-
Routine visits and monitoring	£3,311.58	£2,636.25	£675.33	£675.33	26%
Adverse events	£325.80	£0.00	£325.80	£325.80	-
Vision loss: Community care	£229.12	£502.22	-£273.09	£273.09	54%
Vision loss: Residential care	£2,903.16	£6,363.43	-£3,460.27	£3,460.27	54%
Vision loss: Depression	£110.57	£242.35	-£131.78	£131.78	54%
Vision loss: Hip replacement	£151.88	£332.91	-£181.03	£181.03	54%
Total	**£9,788**	**£10,077**	**-£289**	**£289**	**3%**