Additional analysis commissioned by the NHS R&D HTA Programme on behalf of the National Institute for Health and Clinical Excellence

Ranibizumab and pegaptanib for the treatment of age-related macular degeneration: further analysis requested by NICE in response to consultation on ACD

Produced by Southampton Health Technology Assessments Centre

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None

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The views expressed in this report are those of the authors and not necessarily those of the NHS R&D HTA Programme. Any errors are the responsibility of the authors.

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Models of second eye treatment in AMD.

Question 1: To give an indication of the range of ICERs to be expected if both eyes are treated (or if only one eye is affected, treatment of that eye without waiting for a second to be affected). What is the expected ICER of treating the whole group of patients (some of whom will first seek medical attention with one eye affected, some with both) with this approach? What are the limitations of the evidence base for the assumptions for utility values in this analysis?

Deliverable(s): To produce an analysis indicating the range of ICERs to be expected if both eyes are treated (or if only one eye is affected, treatment of that eye without waiting for a second to be affected). Given the complex nature of the underlying disease and effects of treatment, the related challenges and barriers to building and interpreting models of treating the worse-seeing eye, and the time constraints between Appraisal Committee meetings, this analysis would be expected to be an indicative/exploratory analysis. The Assessment Group will list any outstanding issues that it has not been able to reflect in the indicative analysis, but considers to be important in interpreting the results. Can sensitivity analyses be presented around the assumptions for utility gain from treating one or the worst-seeing, as opposed to the better-seeing eye only?

Overview

The following section briefly reviews the evidence, with respect to the proportion of patients presenting with their first eye affected and the risk of second eye involvement. We identify major uncertainties in modelling the cost and outcomes of treating one or both eyes and present estimates of the cost implications of treating first and second eyes. We do not present any estimates of the expected outcomes for alternative scenarios of treating one or both eyes. Further work is required to determine the feasibility of modelling outcomes (in terms of visual acuity and quality adjusted life expectancy) and the costs associated with vision loss in patients who receive treatment in one or both eyes.

Assumptions

Proportion presenting with first-eye affected

Widely quoted figures are that 30% to one third of patients currently present with disease in one eye only (the “first eye”). A substantial (i.e. published or fully referenced) source has not been found for this, but responses to ACD included:

- “At present, approximately one third of patients present with first eye.” (RNIB response to ACD)
- “Current data shows that 30% of patients present with wet AMD in the first eye.” (Welsh Assembly Government, though they do not indicate where the data come from).
- “We expect … to develop CNV in NI. Of these 70% will be second eyes ….” (Professor Usha Chakravarthy on behalf of DHSSPSNI).

Risk of second eye involvement

Commonly quoted figure is that 40% of people with CNV in one eye will have second eye involvement within 5 years. We have sought for evidence and found the following:

- Page 1 of PDT TAR[1] states "[A] key issue concerning natural history of wet AMD is that developing the disease in one eye is highly predictive of disease developing in the other eye (up to 42% within 5 years).[2] The original reference for this estimate appears to be a publication from the Macular Photocoagulation Study Group[3]. Pieramici and Bressler[2] quote annual incidence for second eye involvement from 4% to 12%. Five year risk of CNV in second eye ranges from 7% in subgroup with no risk factors to 87% for those with four risk factors (presence of five or more drusen (rr = 2.1), focal hyperpigmentation (rr = 2.0), 1 or more large drusen (rr = 1.5) and definite systemic hypertension (rr = 1.7) [see Arch Ophthalmol, 1997 115(6):741-747].
- The Royal College of Ophthalmologists. Age related macular degeneration. Guidelines. February 2000[4], state "With AMD-related visual loss affecting one eye the risk of losing vision in the fellow eye increases to between 7 and 10% annually (referencing the following publications[5-7]). The five year risk is lowest in the absence of large drusen or pigment hyperplasia but increases with one of these risk factors to 30% or with both to over 50%.[8] The highest risk is for those with a pigment epithelial tear in one eye for whom the annual risk of second eye involvement is closer to 40%.[9]
- For people with advanced AMD in one eye, 5-year risk for developing advanced AMD in the second eye was 14.8%, 35.4% and 53.1% for patients with 2, 3 or 4 risk factors respectively.[10] In this study two risk factors were assigned for the presence of advanced AMD in the first eye and additional risk factors were added for presence of large drusen and/or pigment abnormalities in the eye at risk.

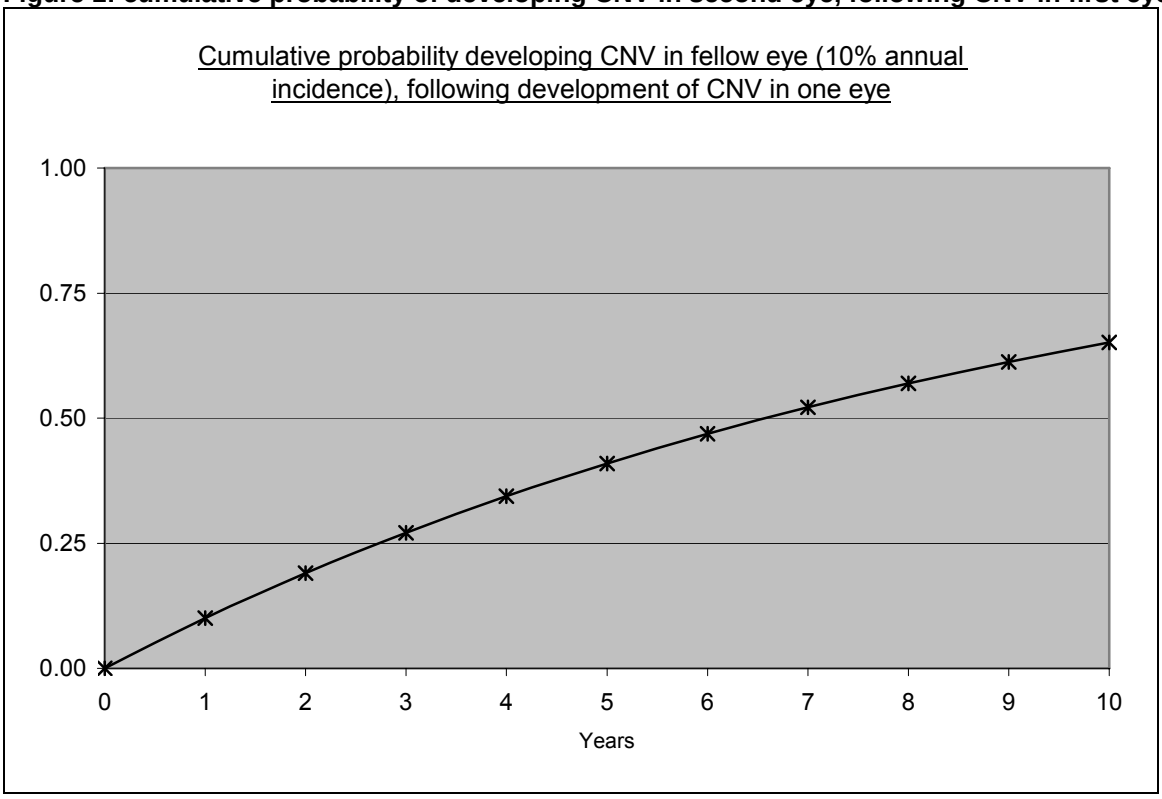
An annual incidence of 10%, which corresponds to 41% at 5 years (see Figure 1), will be used for the cost estimates.

Proportion of second eyes suitable for treatment

Need to consider issue raised by DH:

> *In making the draft recommendation that treatment be for the better seeing eye only, is NICE satisfied that it has considered and given appropriate weight to evidence on the likelihood of a patient developing AMD in their second eye and the probability of developing a treatable form? Has NICE assessed the risk of AMD in the second eye not being treatable, whilst AMD in the first eye could have been (but was not) treated?*

Figure 1: cumulative probability of developing CNV in second eye, following CNV in first eye



Major uncertainties

- How many patients will take up treatment in first eye?
- What happens to patients who develop (treatable) AMD in second eye, while being treated for AMD in first eye? Current assumption is that treatment continues up to two years on first eye then treatment switches to second eye.
- If lesion type in first eye is predominantly classic what is probability that second eye will be minimally classic/ occult no classic?
- What is the procedure for monitoring patients who present with first eye involvement, but get no treatment? Current assumptions are twice yearly out-patient assessment with optometry, OCT and fluoroscein angiography.
- What is the probability that AMD developing in the second eye will be of a treatable form?

An exploration of the cost implications of first eye and second eye presentation.

Treatment with pegaptanib

Table 1 reports estimated costs for alternative treatment strategies for patients presenting with CNV in the first eye. The modelled treatment strategies are to treat both eyes (i.e. treat current CNV with up to two years of pegaptanib and then treat CNV in second eye if it develops). The alternative strategy is to leave the first eye and only treat

once CNV develops in second eye – assuming a 10% risk of second eye involvement for those with CNV in the first eye. Under these assumptions 38% of the original cohort develop CNV in their second eye within five years (41% of patients who survive five years have developed CNV in their second eye). These costs assume that all first and second eyes are eligible for treatment, and all eligible patients accept treatment.

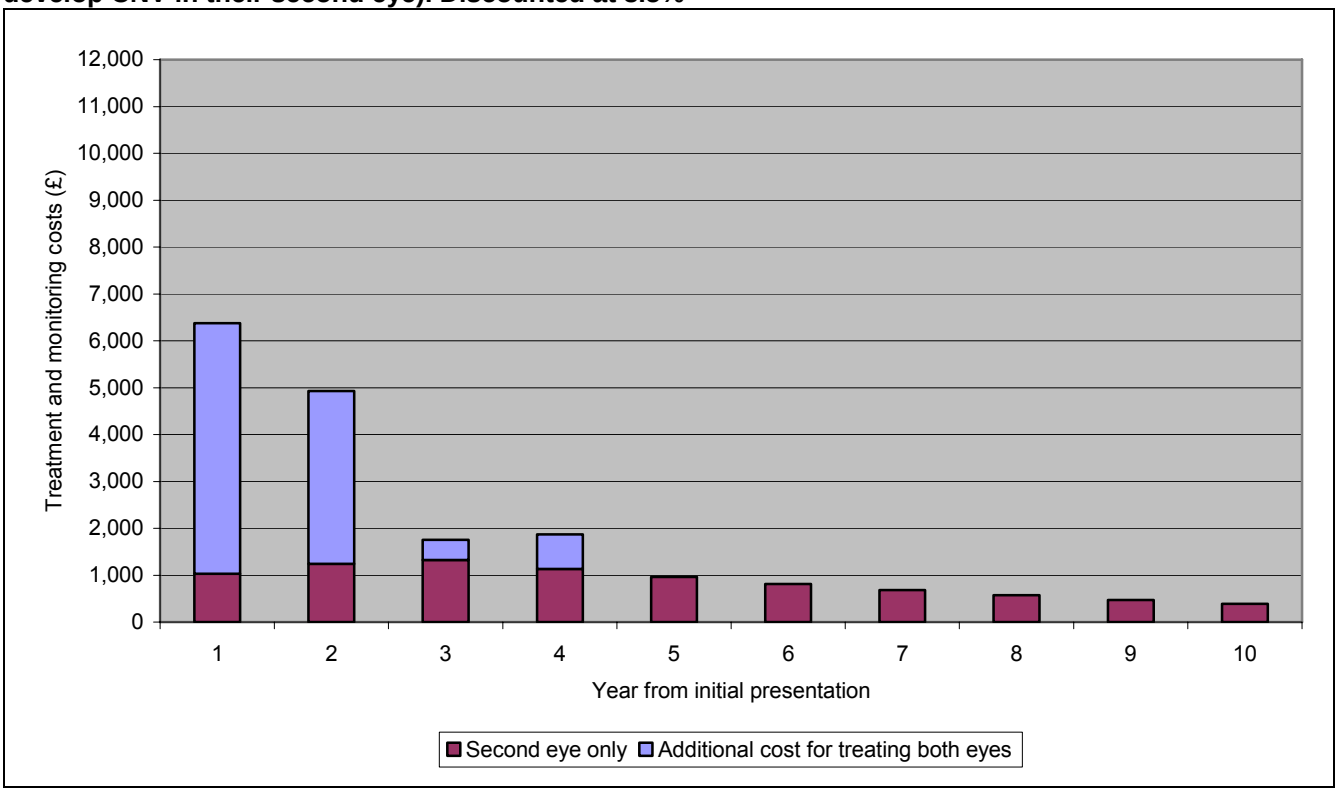
Table 1: pegaptanib treatment costs for alternative treatment strategies for patients presenting with AMD in first eye – accounting for mortality

Number of injections	Treatment strategy	First eye	Second eye	Monitoring costs	Total	Cost difference
Yr1 = 8.4 Yr2 = 6.9	Treat both eyes	11,134	5,301	1,366	17,802	9,974
	Treat second eye only	0	5,373	2,455	7,828	
Yr1 = 9 Yr2 = 8	Treat both eyes	12,072	5,752	1,366	19,190	10,905
	Treat second eye only	0	5,830	2,455	8,285	

Treatment costs in this model are those applied in the base case analysis in the assessment report – i.e. the injection has been costed as an out-patient procedure. Sensitivity analyses will be presented for costing the injection as a day case procedure and also using the costs presented in the Royal College of Ophthalmologists commissioning guidance.

In this model we assume that patients who present for treatment with CNV in their first eye are monitored for development of disease in their fellow eye, given the high probability that those patients will develop CNV in their second eye (as discussed earlier). We assume that all patients will attend twice a year for a vision assessment, OCT and fluoroscein angiography on their second eye, regardless of whether their first eye was treated. The cost associated with this level of monitoring of disease progression in the fellow eye is labelled as “monitoring costs” in Table 1. Treatment costs consist of drug acquisition costs, the injection procedure, plus OCT, vision and medical assessments with fluoroscein angiography every six months on the treated eye.

Figure 2: pegaptanib treatment cost distribution over time for different strategies (assuming 6 weekly assessment and injections over two years for the first eye and for those patients who develop CNV in their second eye). Discounted at 3.5%



Impact of alternative assumptions

Injection costed as a day case procedure

Table 2 shows that the cost difference between the two strategies increases by around 40% if the injection procedure is costed as day case rather than an outpatient procedure.

Table 2: pegaptanib treatment costs for alternative treatment strategies for patients presenting with AMD in first eye – accounting for mortality. Injection costed as a day case procedure

Number of injections	Treatment strategy	First eye	Second eye	Monitoring costs	Total	Cost difference
Yr1 = 8.4 Yr2 = 6.9	Treat both eyes	15,458	7,360	1,366	24,185	14,270
	Treat second eye only	0	7,461	2,455	9,915	
Yr1 = 9 Yr2 = 8	Treat both eyes	16,869	8,038	1,366	26,273	15,671
	Treat second eye only	0	8,147	2,455	10,602	

Royal College of Ophthalmologists Commissioning Guidance Costings

Table 3 shows a similar pattern as Table 2, with cost difference between the two strategies increasing by around 40-50%.

Table 3: pegaptanib treatment costs for alternative treatment strategies for patients presenting with AMD in first eye – accounting for mortality. Treatment costed using Royal College of Ophthalmologists Commissioning Guidance values

Number of injections	Treatment strategy	First eye	Second eye	Monitoring costs	Total	Cost difference
Yr1 = 8.4 Yr2 = 6.9	Treat both eyes	15,866	7,555	1,366	24,788	14,675
	Treat second eye only	0	7,658	2,455	10,113	
Yr1 = 9 Yr2 = 8	Treat both eyes	16,809	8,009	1,366	26,184	15,612
	Treat second eye only	0	8,118	2,455	10,572	

Intensity of monitoring

Table 4 shows that increasing the intensity of monitoring reduces the cost difference between the two strategies, although the difference is marginal (around 8%).

Table 4: pegaptanib treatment costs for alternative treatment strategies for patients presenting with AMD in first eye – accounting for mortality. Quarterly monitoring of disease progression in second eye

Number of injections	Treatment strategy	First eye	Second eye	Monitoring costs	Total	Cost difference
Yr1 = 8.4 Yr2 = 6.9	Treat both eyes	11,134	5,301	2,732	19,168	9,145
	Treat second eye only	0	5,373	4,649	10,023	
Yr1 = 9 Yr2 = 8	Treat both eyes	12,072	5,752	2,732	20,556	10,077
	Treat second eye only	0	5,830	4,649	10,479	

Treatment with ranibizumab

Table 5 reports estimated costs for alternative treatment strategies of treating both eyes, or the second eye only, for patients presenting with CNV in the first eye treated with ranibizumab.

Table 5: ranibizumab treatment costs for alternative treatment strategies for patients presenting with AMD in first eye – accounting for mortality

Number of injections	Treatment strategy	First eye	Second eye	Monitoring costs	Total	Cost difference
Yr1 = 12 Yr2 = 12	Treat both eyes	22,780	10,870	1,366	35,016	21,543
	Treat second eye only	0	11,018	2,455	13,473	
Yr1 = 9 Yr2 = 9	Treat both eyes	18,061	8,618	1,366	28,046	16,855
	Treat second eye only	0	8,736	2,455	11,191	
Yr1 = 9 Yr2 = 6	Treat both eyes	15,796	7,512	1,366	24,674	14,605
	Treat second eye only	0	7,614	2,455	10,069	
Yr1 = 5.6 Yr2 = 5.6	Treat both eyes	12,714	6,067	1,366	20,147	11,543
	Treat second eye only	0	6,149	2,455	8,604	
Yr1 = 6.5 Yr2 = 3.3	Treat both eyes	11,864	5,636	1,366	18,866	10,699
	Treat second eye only	0	5,712	2,455	8,167	

Treatment costs in this model are those applied in the base case analysis in the assessment report. The table presents five different scenarios, in which the number of

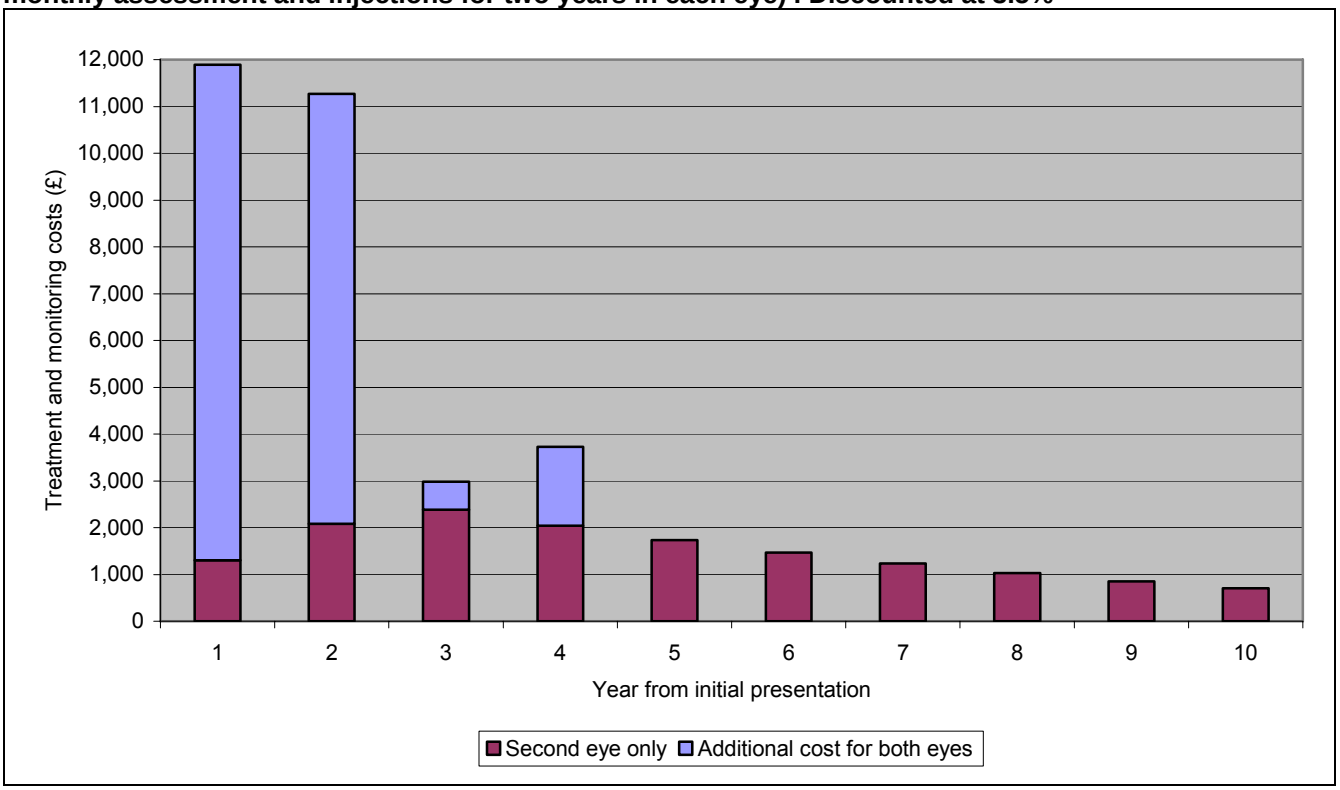
intravitreal injections is varied. The first three scenarios (12 injections in Year 1 and Year 2, 9 injections in Year 1 and Year 2, and 9 injections in Year 1 with 6 injections in Year 2) were included in the deterministic sensitivity analyses included in the assessment report (see Tables 4.29, 4.30 and 4.31 on pages 145 to 147). Monthly injections corresponds to the treatment frequency in the pivotal trials, that provided evidence of efficacy for ranibizumab[11;12]. Evidence submitted by the manufacturer, in support of the ranibizumab submission to NICE, included a disease and dosage schedule model that suggested that a reduced frequency of injection could achieve outcomes equivalent to those observed in the pivotal trials. These supported a dose frequency of 9 in year 1 and 6 in year 2.

The estimate of 5.6 injections in year 1 was derived from the published reports on the PRONTO study[13] which investigated the effectiveness of a reduced dosing schedule, using an “as required” protocol rather than the fixed dosing schedule adopted in the PIER study. The PRONTO study has only published data up to 1 year – hence the same value (5.6 injections is applied to year 2). PRONTO is a small (n=40), uncontrolled observational study and it remains to be seen whether the early findings from that study will be confirmed by the larger (n=600) SUSTAIN study that is currently recruiting and aims to provide additional data on effectiveness of a reduced dosing protocol and frequency of drug administration.

The final scenario in the table is based on information supplied by the manufacturer during consultation on the ACD, which stated that results up to 2 years in the PRONTO study gave a mean number of injections of 9.9 over 2 years – these data do not seem to be published. This number of injections was distributed across each year of treatment based on responses to a survey of ophthalmologists with experience of treating patients with ranibizumab, reported by the manufacturer. This suggested that 58% of patients would receive between 3 to 6 injections over twelve months and 38% would receive between 6 and 12 injections. These are the least evidence-based estimates of frequency of treatment under the reduced frequency protocol and fall well below the values adopted in the Royal College of Ophthalmologists commissioning guidance (8 in year 1 and 6 in year 2).

Figure 3 shows the distribution of treatment costs over time for patients presenting with CNV in their first eye. The bars with the darker shading show costs for treating disease in patients’ second eye (51% of the cohort over 10 year time horizon). The lighter shaded bars show the additional costs associated with treating patients’ first eyes.

Figure 3: ranibizumab treatment cost distribution over time for different strategies (assuming monthly assessment and injections for two years in each eye) . Discounted at 3.5%



Impact of alternative assumptions

Injection costed as a day case procedure

Table 6 shows that costing injection as a day case procedure increases cost by approximately 30% where 12 injections are administered per year. The increase is slightly lower for the reduced frequency dosing regimes.

Table 6: ranibizumab treatment costs for alternative treatment strategies for patients presenting with AMD in first eye – accounting for mortality. Injection costed as a day case procedure

Number of injections	Treatment strategy	First eye	Second eye	Monitoring costs	Total	Cost difference
Yr1 = 12 Yr2 = 12	Treat both eyes	29,536	14,095	1,366	44,997	28,255
	Treat second eye only	0	14,287	2,455	16,741	
Yr1 = 9 Yr2 = 9	Treat both eyes	23,129	11,037	1,366	35,532	21,890
	Treat second eye only	0	11,187	2,455	13,642	
Yr1 = 9 Yr2 = 6	Treat both eyes	20,052	9,534	1,366	30,952	18,834
	Treat second eye only	0	9,664	2,455	12,119	
Yr1 = 5.6 Yr2 = 5.6	Treat both eyes	15,867	7,571	1,366	24,805	14,675
	Treat second eye only	0	7,674	2,455	10,129	
Yr1 = 6.5 Yr2 = 3.3	Treat both eyes	14,713	6,986	1,366	23,065	13,529
	Treat second eye only	0	7,081	2,455	9,536	

Royal College of Ophthalmologists Commissioning Guidance Costings

Table 7 shows that, as was the case with pegaptanib, using the Royal College of Ophthalmologists costs gives very similar results as using the day case procedure cost.

Table 7: ranibizumab treatment costs for alternative treatment strategies for patients presenting with AMD in first eye – accounting for mortality. Treatment costed using Royal College of Ophthalmologists Commissioning Guidance values

Number of injections	Treatment strategy	First eye	Second eye	Monitoring costs	Total	Cost difference
Yr1 = 12 Yr2 = 12	Treat both eyes	29,859	14,250	1,366	45,475	28,576
	Treat second eye only	0	14,444	2,455	16,899	
Yr1 = 9 Yr2 = 9	Treat both eyes	25,121	11,989	1,366	38,476	23,869
	Treat second eye only	0	12,152	2,455	14,607	
Yr1 = 9 Yr2 = 6	Treat both eyes	22,846	10,877	1,366	35,089	21,609
	Treat second eye only	0	11,026	2,455	13,480	
Yr1 = 5.6 Yr2 = 5.6	Treat both eyes	19,751	9,426	1,366	30,543	18,534
	Treat second eye only	0	9,554	2,455	12,009	
Yr1 = 6.5 Yr2 = 3.3	Treat both eyes	18,897	8,993	1,366	29,256	17,686
	Treat second eye only	0	9,116	2,455	11,570	

Intensity of monitoring

Table 8 shows that an increased intensity of monitoring for patients, to detect disease in their second eye, marginally reduces the difference in cost between strategies.

Table 8: ranibizumab treatment costs for alternative treatment strategies for patients presenting with AMD in first eye – accounting for mortality. Quarterly monitoring of disease progression in second eye

Number of injections	Treatment strategy	First eye	Second eye	Monitoring costs	Total	Cost difference
Yr1 = 12 Yr2 = 12	Treat both eyes	22,780	10,870	2,732	36,382	20,714
	Treat second eye only	0	11,018	4,649	15,668	
Yr1 = 9 Yr2 = 9	Treat both eyes	18,061	8,618	2,732	29,412	16,027
	Treat second eye only	0	8,736	4,649	13,385	
Yr1 = 9 Yr2 = 6	Treat both eyes	15,796	7,512	2,732	26,040	13,777
	Treat second eye only	0	7,614	4,649	12,264	
Yr1 = 5.6 Yr2 = 5.6	Treat both eyes	12,714	6,067	2,732	21,513	10,715
	Treat second eye only	0	6,149	4,649	10,799	
Yr1 = 6.5 Yr2 = 3.3	Treat both eyes	11,864	5,636	2,732	20,232	9,870
	Treat second eye only	0	5,712	4,649	10,362	

Alternative assumptions for costs of blindness, treatment cost and frequency of injection with ranibizumab

Question 2: How would estimation of cost effectiveness be affected by alternative assumptions of administration costs as suggested at consultation (e.g. based on the Royal College of Ophthalmologists Commissioning Contemporary Services guide July 2007)

Deliverable(s): To produce ICERs from the AG model using alternative assumptions reflecting the views expressed through consultation with regard to unit costs and resource use assumptions which include the costs of:
Unit costs and resource use related to blindness e.g. costs of falls, hip fractures etc. Levels of uptake of blind related services. It may be ideal to report a sensitivity analysis on these issues.
Costs of administering the injections (day case procedure versus outpatient or an estimate in between based on the RCOphth guide)
The number of injections used for ranibizumab treatment within its licensed indications. This would require assumptions about the percentage of patients who, despite reduced frequency injections, experience the same level of treatment effect as in the ranibizumab studies with monthly injections (MARINA and ANCHOR).

Overview

The following section briefly reviews the evidence, with respect to costs of blindness (and the proportion that each component of blindness costs contributed to total costs) presented in the assessment report and reports sensitivity analyses on key parameters, identified by consultees, as meriting further consideration. This analysis presents the incremental cost per QALY gained under the alternative scenarios.

An important issue to consider here is which costs identified by consultees are associated with AMD (at all levels of vision) or are specific to blindness. For example, the RNIB indicated that people with low vision due to AMD would still attend for clinic visits and optician visits. However these costs are relevant for all people with AMD and are not specific to those whose vision has deteriorated.

We also present sensitivity analyses using alternative costing assumptions: costing visits using unit costs adopted by the Royal College of Ophthalmologists in their commissioning guidance, and also using a weighted combination of outpatient and day case procedure costs for costing the intravitreal injection procedure. Further sensitivity analyses are presented for the reduced frequency dosage regime with ranibizumab. These analysis presents the incremental cost per QALY gained under the alternative scenarios.

Costs of blindness

Appendix A to this report gives some background on the costs of blindness included in the models developed for the assessment report, indicating the proportion of total costs of blindness which were assumed to be one-off and those which are recurrent costs. The one-off and recurrent costs are further broken down by categories of costs.

Unit costs and resource use related to blindness

The majority of comments related to uptake of services for visual impairment and the assumption that certain costs are one-off, rather than unit costs. The following analyses investigate the sensitivity of incremental cost and ICER to alternative assumptions over the uptake of services in the light of comments from consultees and the evidence offered.

Table 9 reports the variables considered in the sensitivity analysis, the values adopted in the base case, those adopted in the sensitivity analysis and the source for the alternative assumption.

Table 9: base case assumption and the assumption adopted in the SA

	Base case value	Value in sensitivity analysis	Source
Proportion registering blind who were previously registered partially sighted	0.00	0.45	RNIB
Proportion having annual re-assessment by OT	0.00	1.00	RNIB
Proportion having annual re-assessment by OT and repeat low vision rehabilitation each year	0.00 0.00	1.00 0.50	RNIB Assumed
Proportion having annual re-assessment by OT and new low vision aids each year	0.00 0.00	1.00 0.50	RNIB Assumed
Uptake of low vision rehabilitation	0.11	0.44	Lotery and colleagues[14]
Uptake of low vision aids	0.33	0.47	
Proportion receiving community care services	0.06	0.25	
Proportion receiving community care services (home care)	0.06	0.17	

Assumptions in the table that show low vision rehabilitation and low vision aids being provided to patients in years after they develop blindness (assumption that patients receive new low vision rehabilitation and new low vision aids every two years) moves these components of costs away from being one-off costs only, to where there is initial assessment and service provision, to allow for these to be included also under the recurrent costs attributed to blindness.

The sensitivity analyses presented below in Table 10 to Table 13 suggest that incremental cost, and hence the ICER, are comparatively insensitive to variation in uptake of services that were suggested as being under-estimated at consultation. The

incremental cost, and ICER were sensitive to alternative assumptions regarding the proportion of blind people receiving community care support. However the values adopted in this sensitivity analysis (25% and 17%) were taken from a study which was not clear on the perspective adopted for costing and which does not report the proportion of domicillary that was funded via social services, rather than funded by service users privately or through allowances. Meads and Hyde[15] noted, in their discussion of their cost of blindness estimates that the proportion of blind people receiving community care support may be higher than their 6% estimate, but adopted this as their most likely estimate due to the proportion of service users funding care privately or through attendance allowances.

Pegaptanib-treated cohort compared with usual care

Table 10: sensitivity analysis for assumptions on uptake of services in costs of blindness for pegaptanib-treated cohort

Variable	Incremental cost	Incremental QALYs	ICER
Proportion of blind registrations previously registered partially sighted (uptake = 0.45)	8,059	0.26	30,973
Annual reassessment by OT	8,031	0.26	30,864
Annual reassessment by OT and LVR every 2 years	7,994	0.26	30,726
Annual reassessment by OT and LVA every 2 years	8,008	0.26	30,779
Change cost of LVR (uptake = 0.44)	8,056	0.26	30,963
Change cost of LVA (uptake = 0.47)	8,061	0.26	30,981
Change cost of CC (uptake = 0.25)	7,273	0.26	27,951
Change cost of CC (uptake = 0.17)	7,605	0.26	29,229

Predominantly classic lesions treated with ranibizumab, compared with PDT.

Table 11: sensitivity analysis for assumptions on uptake of services in costs of blindness for patients with predominantly classic lesions treated with ranibizumab for one year, compared with PDT

Variable	Incremental cost	Incremental QALYs	ICER
Proportion of blind registrations previously registered partially sighted (uptake = 0.45)	5,387	0.34	15,629
Annual reassessment by OT	5,359	0.34	15,546
Annual reassessment by OT and LVR every 2 years	5,323	0.34	15,442
Annual reassessment by OT and LVA every 2 years	5,337	0.34	15,482
Change cost of LVR (uptake = 0.44)	5,385	0.34	15,621
Change cost of LVA (uptake = 0.47)	5,389	0.34	15,634
Change cost of CC (uptake = 0.25)	4,603	0.34	13,354
Change cost of CC (uptake = 0.17)	4,935	0.34	14,315

Predominantly classic lesions treated with ranibizumab, compared with BSC.

Table 12: sensitivity analysis for assumptions on uptake of services in costs of blindness for patients with predominantly classic lesions treated with ranibizumab for one year, compared with BSC

Variable	Incremental cost	Incremental QALYs	ICER
Proportion of blind registrations previously registered partially sighted (uptake = 0.45)	6,452	0.57	11,402
Annual reassessment by OT	6,399	0.57	11,309
Annual reassessment by OT and LVR every 2 years	6,332	0.57	11,191
Annual reassessment by OT and LVA every 2 years	6,358	0.57	11,236
Change cost of LVR (uptake = 0.44)	6,448	0.57	11,395
Change cost of LVA (uptake = 0.47)	6,455	0.57	11,408
Change cost of CC (uptake = 0.25)	5,003	0.57	8,842
Change cost of CC (uptake = 0.17)	5,615	0.57	9,923

Minimally classic and occult no classic lesions treated with ranibizumab.

Table 13: sensitivity analysis for assumptions on uptake of services in costs of blindness for patients with minimally classic and occult no classic lesions treated with ranibizumab

Variable	Incremental cost	Incremental QALYs	ICER
Proportion of blind registrations previously registered partially sighted (uptake = 0.45)	17,299	0.69	25,084
Annual reassessment by OT	17,245	0.69	25,006
Annual reassessment by OT and LVR every 2 years	17,173	0.69	24,901
Annual reassessment by OT and LVA every 2 years	17,201	0.69	24,941
Change cost of LVR (uptake = 0.44)	17,292	0.69	25,073
Change cost of LVA (uptake = 0.47)	17,305	0.69	25,092
Change cost of CC (uptake = 0.25)	15,730	0.69	22,808
Change cost of CC (uptake = 0.17)	16,394	0.69	23,772

Cost of assessment and treatment as per Royal College of Ophthalmologists commissioning guidance

Treatment costs presented in the Royal College of Ophthalmologists commissioning guidance (reproduced in Table 14) need to be adjusted in order to be consistent with NICE methodological guidance for technology appraisal and to allow for the calculation of the cost of an assessment only visit, i.e. without injection. Specifically, we need to remove VAT from drug cost, see Table 15 and Table 16. This in combination with the

20% overhead applied to all costs (including the post-VAT drug cost) increases the cost per visit by between 18% and 24%, depending on the drug and the type of visit.

Table 14: costs of treatment with pegaptanib and ranibizumab as reported in Royal College of Ophthalmologists commissioning guideline

	ranibizumab		pegaptanib	
	Full Assessment	Injection Only	Full Assessment	Injection Only
Staffing	£230.00	£172.00	£230.00	£172.00
Band 7 Management	£44.00	£44.00	£44.00	£44.00
Other Drugs	£8.00	£8.00	£8.00	£8.00
Non Pay Costs	£92.00	£92.00	£92.00	£92.00
FFA	£35.00		£35.00	
OCT	£14.00	£14.00	£14.00	£14.00
Intraocular Pressure	£2.00	£2.00	£2.00	£2.00
Incidentals	£111.00	£111.00	£111.00	£111.00
PTS	£28.00	£28.00	£28.00	£28.00
Total for visit	***£564.00***	***£471.00***	***£564.00***	***£471.00***
Drug (with VAT at 17.5% added)	£894.41	£894.41	£604.00	£604.00
Sub-total	***£1,458.41***	***£1,365.41***	***£1,168.00***	***£1,075.00***
Overheads @ 20%	£291.68	£273.08	£233.60	£215.00
Cost per patient	***£1,750.09***	***£1,638.49***	***£1,401.60***	***£1,290.00***

Removing VAT on drug costs reduces the cost of a full assessment (which includes fluoroscein angiography) including treatment with ranibizumab from £1,401.60 to £1190.80 (15% reduction) and reduces the cost of an injection only visit from £1,290 to £1,079.20 (16% reduction).

Table 15: adjustments to the pegaptanib treatment costs reported in the Royal College of Ophthalmologists commissioning guidance for use in the model

Cost item	Full assessment (£)	Injection only (£)
Non-drug costs (see the item "Total for visit in Table 14)	564.00	471.00
Drug costs	514.00	514.00
20% Trust overhead on all costs and VAT (17.5%) on drug costs ("Cost per patient" in Table 14)	1,401.60	1,290.00
20% Trust overhead on all costs but no VAT on drug costs	1,293.60	1,182.00
20% Trust overhead on non-drug costs only, no VAT on drug costs	1,190.80	1,079.20

Removing VAT on drug costs reduces the cost of a full assessment (which includes fluoroscein angiography) including treatment with ranibizumab from £1,750.09 to £1,438 (18% reduction) and reduces the cost of an injection only visit from £1638.49 to £1326.40 (19% reduction).

Table 16: adjustments to the ranibizumab treatment costs reported in the Royal College of Ophthalmologists commissioning guidance for use in the model

Cost item	Full assessment (£)	Injection only (£)
Non-drug costs (see the item "Total for visit in Table 14)	564.00	471.00
Drug costs	761.20	761.20
20% Trust overhead on all costs and VAT (17.5%) on drug costs	1,750.09	1,638.49
20% Trust overhead on all costs but no VAT on drug costs	1,590.24	1,478.64
20% Trust overhead on non-drug costs only, no VAT on drug costs	1,438.00	1,326.40

For this report we also need to estimate a cost for clinic attendance, without injection – to be able to cost the reduced dosage protocols suggested for ranibizumab. One approach to this would be to simply exclude the drug costs for assessment only visits and use the total of non-drug costs (£564 for full assessment and £471 for "injection only visits). It is likely that other cost items in Table 14 also relate directly to the injection procedure, but it is not apparent which these may be. We have contacted the team who originally produced these costings. However they have not been able to rework the costings to estimate an assessment only visit in the time available. For the purpose of this report we have excluded "Non-pay costs" (£92.00) to derive a cost for a visit where no injection procedure takes place, see Table 17.

For the current report we have assumed that all patients have a full assessment every three months – they have a fluoroscein angiography and greater staffing input at these visits. Staff cost (under the heading "Staffing") is 34% higher on the full assessment visits than for the "injection only" visit. This corresponds to fluoroscein angiography every three months, similar to the protocol for PDT. A sensitivity analysis is presented using full assessment every six months.

Table 17: estimates for clinic visit without injection, based on costs in RCOphth commissioning guidance

Cost item	Full assessment (£)	"Injection only" (£)
Non-drug costs from Table 14	564.00	471.00
Non-drug costs (excluding "Non-pay" costs as an estimate of an assessment only visit)	472.00	379.00
20% Trust overhead on non-drug costs only (excluding "Non-pay" costs)	566.40	454.80

Pegaptanib-treated cohort compared with usual care

Applying VISION study outcomes without assessment of disease modifying effect

Incremental costs and ICERs using treatment costs presented in the Royal College of Ophthalmologists commissioning guidance, with the adjustments described above are reported in Table 18 below. Results are presented for each of the scenarios, with regard to the number of injections, included in the deterministic sensitivity analyses in the assessment report (Table 4.24, page 135-6).

Table 18: applying pegaptanib treatment costs presented in the Royal College of Ophthalmologists commissioning guidance

Strategy	Incremental cost (£)	Incremental QALYs	ICER (£)
Base case	8,062	0.26	30,986
Base case (day case procedure)	12,449	0.26	47,845
Royal College of Ophthalmologists costs			
8.4 injections in yr 1, 6.9 in yr 2	13,180	0.26	50,654
9 injections in yr 1, 6.9 in yr 2	13,552	0.26	52,084
8.4 injections in yr 1, 8 in yr 2	13,796	0.26	53,022
9 injections in yr 1, 8 in yr 2	14,168	0.26	54,452

A breakdown of the base case costs (8.4 injections in year 1 and 6.9 in year 2) by major categories for the analysis using alternative unit cost assumptions is shown in Table 19.

Table 19: breakdown of pegaptanib treatment costs for each cohort by major categories. Using assessment group and Royal College of Opthalmologists unit costs

		Drug	Admin and Monitoring	Adverse events	PDT	Blindness
AG (OP proc)	UC	0	220	0	590	15,789
	Peg	7,388	4,107	98	404	12,666
AG (day case)	UC	0	220	0	590	15,789
	Peg	7,388	8,493	98	404	12,666
RCOphth	UC	0	220	0	590	15,789
	Peg	7,388	9,224	98	404	12,666

The analysis presented in Table 18 and Table 19 are based on a schedule of a full assessment every three months. A further analysis is presented based on a schedule of a full assessment (which includes fluoroscein angiography) every six months (see Table 20), rather than every three months.

Table 20: applying pegaptanib treatment costs presented in the Royal College of Ophthalmologists commissioning guidance – full assessment every six months

Strategy	Incremental cost (£)	Incremental QALYs	ICER (£)
8.4 injections in yr 1, 6.9 in yr 2	12,913	0.26	49,628

9 injections in yr 1, 6.9 in yr 2	13,343	0.26	51,283
8.4 injections in yr 1, 8 in yr 2	13,421	0.26	51,581
9 injections in yr 1, 8 in yr 2	13,852	0.26	53,237

Including disease modifying effect for pegaptanib, year 3 only

Table 21 reports incremental costs and ICERs under the assumption that pegaptanib has a disease modifying effect, reducing the proportion of patients having significant loss of vision (as described in the assessment report) for the year following cessation of treatment.

Table 21: applying pegaptanib treatment costs presented in the Royal College of Ophthalmologists commissioning guidance – disease modifying effect in year 3

Strategy	Incremental cost (£)	Incremental QALYs	ICER (£)
Base case	7,710	0.29	26,896
Base case (day case procedure)	12,097	0.29	42,198
Royal College of Ophthalmologists costs			
8.4 injections in yr 1, 6.9 in yr 2	12,827	0.29	44,747
9 injections in yr 1, 6.9 in yr 2	13,199	0.29	46,045
8.4 injections in yr 1, 8 in yr 2	13,444	0.29	46,897
9 injections in yr 1, 8 in yr 2	13,816	0.29	48,194

A breakdown of costs by major categories is shown in Table 22. As would be expected the only category that varies between the three scenarios is “Administration and Monitoring”.

Table 22: breakdown of pegaptanib treatment costs for each cohort by major categories. Using assessment group and Royal College of Opthalmologists unit costs

		Drug	Admin and Monitoring	Adverse events	PDT	Blindness
AG (OP proc)	UC	0	220	0	590	15,789
	Peg	7,388	4,107	98	404	12,314
AG (day case)	UC	0	220	0	590	15,789
	Peg	7,388	8,493	98	404	12,314
RCOphth	UC	0	220	0	590	15,789
	Peg	7,388	9,224	98	404	12,314

Table 23: applying pegaptanib treatment costs presented in the Royal College of Ophthalmologists commissioning guidance – full assessment every six months – with disease modifying effect in year following cessation of treatment

Strategy	Incremental cost (£)	Incremental QALYs	ICER (£)
8.4 injections in yr 1, 6.9 in yr 2	12,560	0.29	43,816

9 injections in yr 1, 6.9 in yr 2	12,991	0.29	45,319
8.4 injections in yr 1, 8 in yr 2	13,069	0.29	45,589
9 injections in yr 1, 8 in yr 2	13,500	0.29	47,092

Including disease modifying effect for pegaptanib, year 3 onwards

Table 24 reports incremental costs and ICERs assuming pegaptanib has a disease modifying effect for the remainder of the model time horizon.

Table 24: applying pegaptanib treatment costs presented in the Royal College of Ophthalmologists commissioning guidance – disease modifying effect for model time horizon

Strategy	Incremental cost (£)	Incremental QALYs	ICER (£)
Base case	6,941	0.34	20,467
Base case (day case procedure)	11,328	0.34	33,401
Royal College of Ophthalmologists costs			
8.4 injections in yr 1, 6.9 in yr 2	12,058	0.34	35,556
9 injections in yr 1, 6.9 in yr 2	12,430	0.34	36,653
8.4 injections in yr 1, 8 in yr 2	12,674	0.34	37,372
9 injections in yr 1, 8 in yr 2	13,046	0.34	38,469

A breakdown of these costs by major categories is shown in Table 25.

Table 25: breakdown of pegaptanib treatment costs for each cohort by major categories. Using assessment group and Royal College of Opthalmologists unit costs

		Drug	Admin and Monitoring	Adverse events	PDT	Blindness
AG (OP proc)	UC	0	220	0	590	15,789
	Peg	7,388	4,107	98	404	11,544
AG (day case)	UC	0	220	0	590	15,789
	Peg	7,388	8,493	98	404	11,544
RCOphth	UC	0	220	0	590	15,789
	Peg	7,388	9,224	98	404	11,544

Table 26: applying pegaptanib treatment costs presented in the Royal College of Ophthalmologists commissioning guidance – full assessment every six months – with disease modifying effect in year following cessation of treatment

Strategy	Incremental cost (£)	Incremental QALYs	ICER (£)
8.4 injections in yr 1, 6.9 in yr 2	11,791	0.34	34,768
9 injections in yr 1, 6.9 in yr 2	12,222	0.34	36,038
8.4 injections in yr 1, 8 in yr 2	12,300	0.34	36,267
9 injections in yr 1, 8 in yr 2	12,730	0.34	37,537

Predominantly classic lesions treated with ranibizumab, compared with PDT.

Incremental costs and ICERs using treatment costs presented in the Royal College of Ophthalmologists commissioning guidance, with the adjustments described above are reported in Table 27 below. Results are presented for each of the scenarios, with regard to the number of injections, included in the deterministic sensitivity analyses in the assessment report (Table 4.29, page 145).

Table 27: applying ranibizumab treatment costs presented in the Royal College of Ophthalmologists commissioning guidance for predominantly classic lesions treated with ranibizumab for one year, compared with PDT

Strategy	Incremental cost (£)	Incremental QALYs	ICER (£)
Base case	5,391	0.34	15,638
Base case (day case procedure)	8,998	0.34	26,102
RCOphth costs (12 injections)	9,195	0.34	26,674
RCOphth costs (9 injections)	6,619	0.34	19,203
RCOphth costs (6.5 injections)	4,473	0.34	12,976
RCOphth costs (5.6 injections)	3,700	0.34	10,735

A breakdown of the base case (12 injections per year) costs by major categories is shown in Table 28.

Table 28: breakdown of ranibizumab treatment costs for each cohort by major categories. Using assessment group and Royal College of Opthalmologists unit costs

		Drug	Admin and Monitoring	Adverse events	PDT	Blindness
AG (OP proc)	PDT	0	0	78	3,845	17,575
	Ran	8,997	3,316	114	0	14,461
AG (day case)	PDT	0	0	78	3,845	17,575
	Ran	8,997	6,923	114	0	14,461
RCOphth	PDT	0	0	78	3,845	17,575
	Ran	8,997	7,120	114	0	14,461

Predominantly classic lesions treated with ranibizumab, compared with BSC.

Incremental costs and ICERs using treatment costs presented in the Royal College of Ophthalmologists commissioning guidance, with the adjustments described above are reported in Table 29 below. Results are presented for each of the scenarios, with regard to the number of injections, included in the deterministic sensitivity analyses in the assessment report (Table 4.30, page 146) and a breakdown by major cost categories is shown in Table 30.

Table 29: applying ranibizumab treatment costs presented in the Royal College of Ophthalmologists commissioning guidance for predominantly classic lesions treated with ranibizumab for one year, compared with BSC

Strategy	Incremental cost (£)	Incremental QALYs	ICER (£)
Base case	6,457	0.57	11,412
Base case (day case procedure)	10,065	0.57	17,787
RCOphth costs (12 injections)	10,262	0.57	18,135
RCOphth costs (9 injections)	7,686	0.57	13,584
RCOphth costs (6.5 injections)	5,540	0.57	9,791
RCOphth costs (5.6 injections)	4,767	0.57	8,425

Table 30: breakdown of ranibizumab treatment costs for each cohort by major categories. Using assessment group and Royal College of Opthalmologists unit costs

		Drug	Admin and Monitoring	Adverse events	PDT	Blindness
AG (OP proc)	BSC	0	221	0	0	20,210
	Ran	8,997	3,316	114	0	14,461
AG (day case)	BSC	0	221	0	0	20,210
	Ran	8,997	6,923	114	0	14,461
RCOphth	BSC	0	221	0	0	20,210
	Ran	8,997	7,120	114	0	14,461

Minimally classic and occult no classic treated with ranibizumab

Incremental costs and ICERs using treatment costs presented in the Royal College of Ophthalmologists commissioning guidance, with the adjustments described above are reported in Table 31 below. Results are presented for each of the scenarios, with regard to the number of injections, included in the deterministic sensitivity analyses in the assessment report (Table 4.31, page 147) and a breakdown by major cost categories is shown in Table 32.

Table 31: applying ranibizumab treatment costs presented in the Royal College of Ophthalmologists commissioning guidance for minimally classic and occult no classic lesions treated with ranibizumab, compared with BSC

Strategy	Incremental cost (£)	Incremental QALYs	ICER (£)
Base case	17,309	0.69	25,098
Base case (day case procedure)	24,246	0.69	35,157
RCOphth costs			
12 injections in yr 1, 12 in yr 2	24,735	0.69	35,866
12 injections in yr 1, 9 in yr 2	22,354	0.69	32,414
9 injections in yr 1, 9 in yr 2	19,779	0.69	28,680

9 injections in yr 1, 6 in yr 2	17,398	0.69	25,227
9 injections in yr 1, 3.5 in yr 2	15,413	0.69	22,349
6.5 injections in yr 1, 3.5 in yr 2	13,268	0.69	19,238

Table 32: breakdown of total costs for each cohort by major categories. Using assessment group and Royal College of Opthalmologists unit costs

		Drug	Admin and Monitoring	Adverse events	PDT	Blindness
AG (OP proc)	BSC	0	220	0	0	13,567
	Ran	17,314	6,275	193	0	7,313
AG (day case)	BSC	0	220	0	0	13,567
	Ran	17,314	13,213	193	0	7,313
RCOphth	BSC	0	220	0	0	13,567
	Ran	17,314	13,702	193	0	7,313

Injection procedure cost based on a combination of outpatient and day case costs

The Novartis economic model assumed (based on a survey of UK ophthalmologists) that 75% of centres would perform intravitreal injections as day cases and 25% would perform them as outpatient procedures. Responses to the ACD were concerned that costing the injection procedure as a day case was adopting a unit cost at the extreme high end of possible values.

If the day case procedure cost is £395 (as in the Novartis submission and as used in the assessment group model) and outpatient cost is £90.20 (as in the assessment group model) the weighted average cost for intravitreal injection is (0.25*90.20) + (0.75*395) = 318.80. This cost has been applied in the assessment group model and results are reported below.

Pegaptanib-treated cohort compared with usual care

Applying VISION study outcomes without assessment of disease modifying effect

For results including those in the assessment report and with the new estimate for procedure cost, see Table 33 below.

Table 33: sensitivity analysis on cost of injection procedure (combination of day case and outpatient procedure cost) for pegaptanib-treated cohort

Strategy	Incremental cost (£)	Incremental QALYs	ICER (£)
Base case	8,062	0.26	30,986
Costed as day case	12,449	0.26	47,845
Costed as per Novartis	11,352	0.26	43,631

Including disease modifying effect for pegaptanib, year 3 only

For results including those in the assessment report and with the new estimate for procedure cost, allowing for a disease modifying effect of pegaptanib in the year following cessation of treatment, see Table 34 below.

Table 34: sensitivity analysis on cost of injection procedure (combination of day case and outpatient procedure cost) for pegaptanib-treated cohort

Strategy	Incremental cost (£)	Incremental QALYs	ICER (£)
Base case	7,710	0.29	26,896
Costed as day case	12,097	0.29	42,198
Costed as per Novartis	11,000	0.29	38,373

Including disease modifying effect for pegaptanib, year 3 onwards

For results including those in the assessment report and with the new estimate for procedure cost, allowing for a disease modifying effect of pegaptanib for the remainder of the model time horizon, see Table 35 below.

Table 35: sensitivity analysis on cost of injection procedure (combination of day case and outpatient procedure cost) for pegaptanib-treated cohort

Strategy	Incremental cost (£)	Incremental QALYs	ICER (£)
Base case	6,941	0.34	20,467
Costed as day case	11,328	0.34	33,401
Costed as per Novartis	10,231	0.34	30,167

Predominantly classic lesions treated with ranibizumab, compared with PDT.

For results including those in the assessment report and with the new estimate for procedure cost, see Table 36 below.

Table 36: sensitivity analysis on cost of injection procedure (combination of day case and outpatient procedure cost) for predominantly classic lesions treated with ranibizumab compared with PDT

Strategy	Incremental cost (£)	Incremental QALYs	ICER (£)
Base case	5,391	0.34	15,638
Costed as day case	8,998	0.34	26,102
Costed as per Novartis	8,096	0.34	23,486

Predominantly classic lesions treated with ranibizumab, compared with BSC.

For results including those in the assessment report and with the new estimate for procedure cost, see Table 37 below.

Table 37: sensitivity analysis on cost of injection procedure (combination of day case and outpatient procedure cost) for predominantly classic lesions treated with ranibizumab compared with BSC

Strategy	Incremental cost (£)	Incremental QALYs	ICER (£)
Base case	6,457	0.57	11,412
Costed as day case	10,065	0.57	17,787
Costed as per Novartis	9,163	0.57	16,193

Minimally classic and occult no classic treated with ranibizumab

For results including those in the assessment report and with the new estimate for procedure cost, see Table 38 below.

Table 38: sensitivity analysis on cost of injection procedure (combination of day case and outpatient procedure cost) for minimally classic and occult no classic lesions treated with ranibizumab

Strategy	Incremental cost (£)	Incremental QALYs	ICER (£)
Base case	17,309	0.69	25,098
Costed as day case	24,246	0.69	35,157
Costed as per Novartis	22,512	0.69	32,642

Reduced frequency dosage regime for ranibizumab

Modifications to the model

It was necessary to amend the model to cost the reduced dosage regime for ranibizumab correctly. The formula in the original model assumed that the optometry, OCT and medical assessments would occur less frequently when the number of injections was reduced. This overestimated the saving, through the reduced frequency dosage regime, since patients should still have monthly assessments, whether or not they have monthly injections. New estimates have been calculated for entries in deterministic sensitivity analysis tables in the assessment report (Tables 4.29 to 4.31, pages 145 to 147 in the assessment report). The following sections report the impact of the changed formula on results already presented in the assessment report (including the reduced frequency regime based on the drug and disease model reported in the manufacturer's submission), and then report the ICER for other suggested reduced frequency dosage regimes.

Predominantly classic lesions treated with ranibizumab, compared with PDT.

Effect of change in formula on base case results – zero. Result in assessment report is incremental cost of £5,391 and incremental QALYs of 0.34 (ICER = £15,638). For results with new formula see Table 39 below.

Effect on sensitivity analysis reported on page 145. Result in assessment report is incremental cost of £2,377 and incremental QALYs of 0.34 (ICER = £6,897). For results with new formula see Table 39 below.

Table 39: sensitivity analysis on number of injections (corrected analysis) for predominantly classic lesions treated with ranibizumab compared with PDT

Strategy	Incremental cost (£)	Incremental QALYs	ICER (£)
Base case	5,391	0.34	15,638
9 injections in year 1	2,875	0.34	8,340
6.5 injections in year 1	778	0.34	2,258
5.6 injections in year 1	24	0.34	69
Notes: 9 was figure in Novartis submission for injections in year 1. 6.5 is based on two year average from the PRONTO study combined with survey of ophthalmologists opinion reported in responses to consultation on ACD. 5.6 is value published in PRONTO publication (American Journal of Ophthalmology. 2007 143(4);566-583.			

Predominantly classic lesions treated with ranibizumab, compared with BSC.

Effect of change in formula on base case results – zero. Result in assessment report is incremental cost of £6,457 and incremental QALYs of 0.57 (ICER = £11,412). For results with new formula see Table 40 below.

Effect on sensitivity analysis reported on page 146. Result in assessment report is incremental cost of £3,444 and incremental QALYs of 0.57 (ICER = £6,087). For results with new formula see Table 40 below.

Table 40: sensitivity analysis on number of injections (corrected analysis) for predominantly classic lesions treated with ranibizumab compared with BSC

Strategy	Incremental cost (£)	Incremental QALYs	ICER (£)
Base case	6,457	0.57	11,412
9 injections in year 1	3,942	0.57	6,966
6.5 injections in year 1	1,845	0.57	3,261
5.6 injections in year 1	1,090	0.57	1,927
Notes: 9 was figure in Novartis submission for injections in year 1. 6.5 is based on two year average from the PRONTO study combined with survey of ophthalmologists opinion reported in responses to consultation on ACD. 5.6 is value published in PRONTO publication (American Journal of Ophthalmology. 2007 143(4);566-583.			

Minimally classic and occult no classic treated with ranibizumab

Effect of change in formula on base case results – zero. Result in assessment report is incremental cost of £17,309 and incremental QALYs of 0.69 (ICER = £25,098). For results with new formula see Table 41 below.

Effect on sensitivity analysis reported on page 147. Result in assessment report for:

- 12 injections in yr 1, 9 in yr 2, is incremental cost of £14,522 and incremental QALYs of 0.69 (ICER = £21,058)
- 9 injections in yr 1, 9 in yr 2, is incremental cost of £11,510 and incremental QALYs of 0.69 (ICER = £16,689)
- 9 injections in yr 1, 6 in yr 2, is incremental cost of £8,723 and incremental QALYs of 0.69 (ICER = £12,649)

For results with new formula see Table 41 below.

Table 41: sensitivity analysis on number of injections (corrected analysis) for minimally classic and occult no classic lesions treated with ranibizumab

Strategy	Incremental cost (£)	Incremental QALYs	ICER (£)
Base case	17,309	0.69	25,098
12 injections in yr 1, 9 in yr 2	14,982	0.69	21,725
9 injections in yr 1, 9 in yr 2	12,467	0.69	18,077
9 injections in yr 1, 6 in yr 2	10,141	0.69	14,704
9 injections in yr 1, 3.5 in yr 2	8,203	0.69	11,894
6.5 injections in yr 1, 3.5 in yr 2	6,106	0.69	8,854
Notes: 9 injections in year 1 and 6 in year 2 were used in Novartis submission. 6.5 in year 1 and 3.5 in year 2 are based on two year average from the PRONTO study combined with survey of ophthalmologists opinion reported in responses to consultation on ACD.			

Additional sensitivity analyses

Additional sensitivity analyses were requested, including alternative estimates for health state utility with respect to visual acuity. Two alternative sets of utility estimates have been included in this analysis:

- firstly those developed by SCHARR for the current submission to NICE in support of ranibizumab.[16] This reference was submitted as Appendix II to the Lucentis NICE submission. These utility values were estimated using the Time Trade Off (TTO) method used to value the EQ-5D;
- secondly those published by Espallargues and colleagues.[17]

The visual acuity states adopted in the SCHARR study were not the same as those used in the assessment group model. To take account of these differences we estimated a simple linear regression model using the mean TTO valuation as

dependent variable and the mean number of letters read (based on the visual acuity range) as the independent variable (see Appendix B for more detail).

The utility values reported by Espallargues and colleagues[17] were estimated using the HUI-3 and valued using data from a Canadian general population sample. The valuations reported by Espallargues and colleagues[17] start from a lower value (0.50 for a visual acuity range of greater than 6/12 (or 20/40 in feet)).

Pegaptanib-treated cohort compared with usual care

Table 42: sensitivity analysis on utility values applied for pegaptanib-treated cohort compared with usual care

		Incremental cost	Incremental QALYs	ICER
Base case		8,062	0.26	30,986
Health state utilities	"Brazier" values	8,062	0.21	38,928
	"Espallargues" values	8,062	0.09	91,712

Predominantly classic lesions treated with ranibizumab, compared with PDT

Table 43: sensitivity analysis on utility values applied for predominantly classic lesions compared with PDT

		Incremental cost	Incremental QALYs	ICER
Base case		5,391	0.34	15,638
Health state utilities	"Brazier" values	5,391	0.28	19,491
	"Espallargues" values	5,391	0.15	36,936

Predominantly classic lesions treated with ranibizumab, compared with BSC

Table 44: sensitivity analysis on utility values applied for predominantly classic lesions compared with BSC

		Incremental cost	Incremental QALYs	ICER
Base case		6,457	0.57	11,412
Health state utilities	"Brazier" values	6,457	0.45	14,388
	"Espallargues" values	6,457	0.21	30,241

Minimally classic and occult no classic lesions treated with ranibizumab

Table 45: sensitivity analysis on utility values applied for minimally classic and occult no classic lesions

		Incremental cost	Incremental QALYs	ICER
Base case		17,309	0.69	25,098
Health state utilities	"Brazier" values	17,309	0.54	31,966
	"Espallargues" values	17,309	0.28	62,103

Projection of treatment effect.

Question 4: Could the projection of treatment of effect assumed in the Assessment Group model be illustrated graphically (particularly in order to compare the assumptions underlying the model based one year trial data (ANCHOR) in the predominantly classic group versus modelling based on two year trial data (in the minimally classic and occult no classic subgroup for ranibizumab and from the VISION study for pegaptanib)?

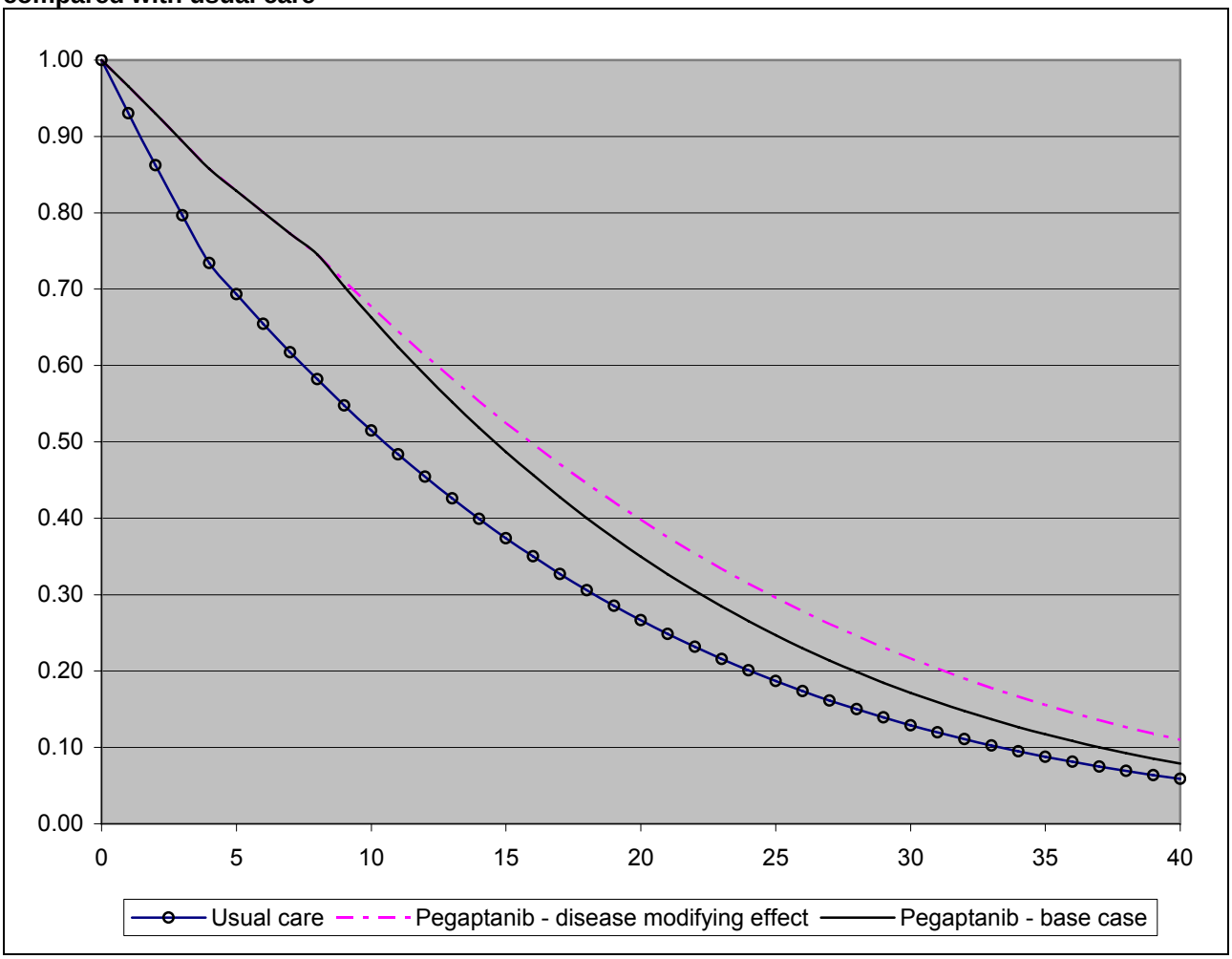
Deliverable(s): (time permitting) Could the projection of treatment of effect assumed in the Assessment Group model be illustrated graphically (particularly in order to compare the assumptions underlying the model based one year trial data (ANCHOR) in the predominantly classic group versus modelling based on two year trial data (in the minimally classic and occult no classic subgroup for ranibizumab and from the VISION study for pegaptanib)?

Graphs "vision survival", i.e. those alive with VA greater than 6/60 over time

The following four charts illustrate assumptions over treatment effects over the trial durations and projections up to 10 years in the treatment and control cohorts. The charts show the proportion of the cohort surviving and with visual acuity in the treated eye greater than 6/60.

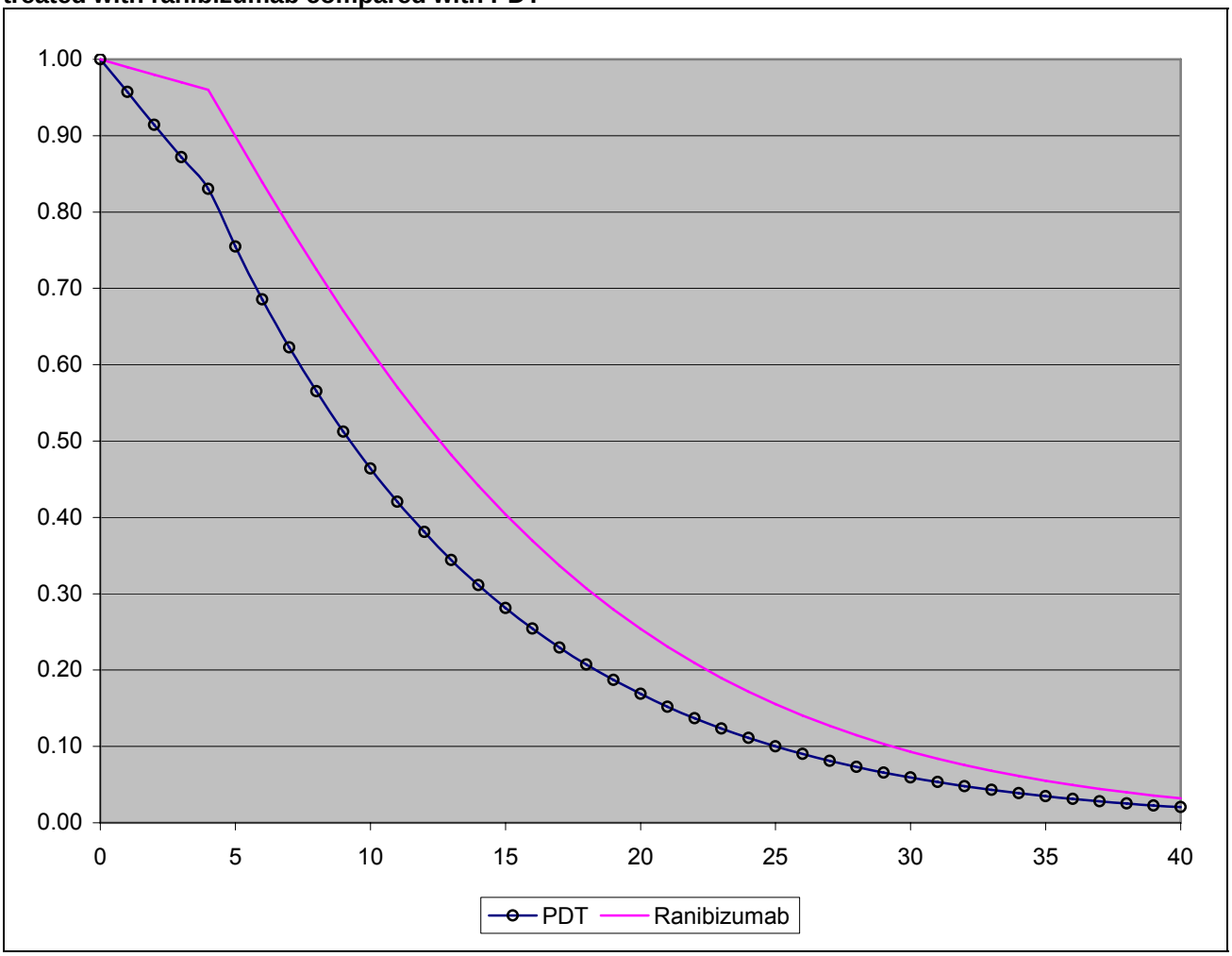
Pegaptanib-treated cohort compared with usual care

Figure 4: proportion of cohort surviving and sighted over 10 years, pegaptanib-treated cohort compared with usual care



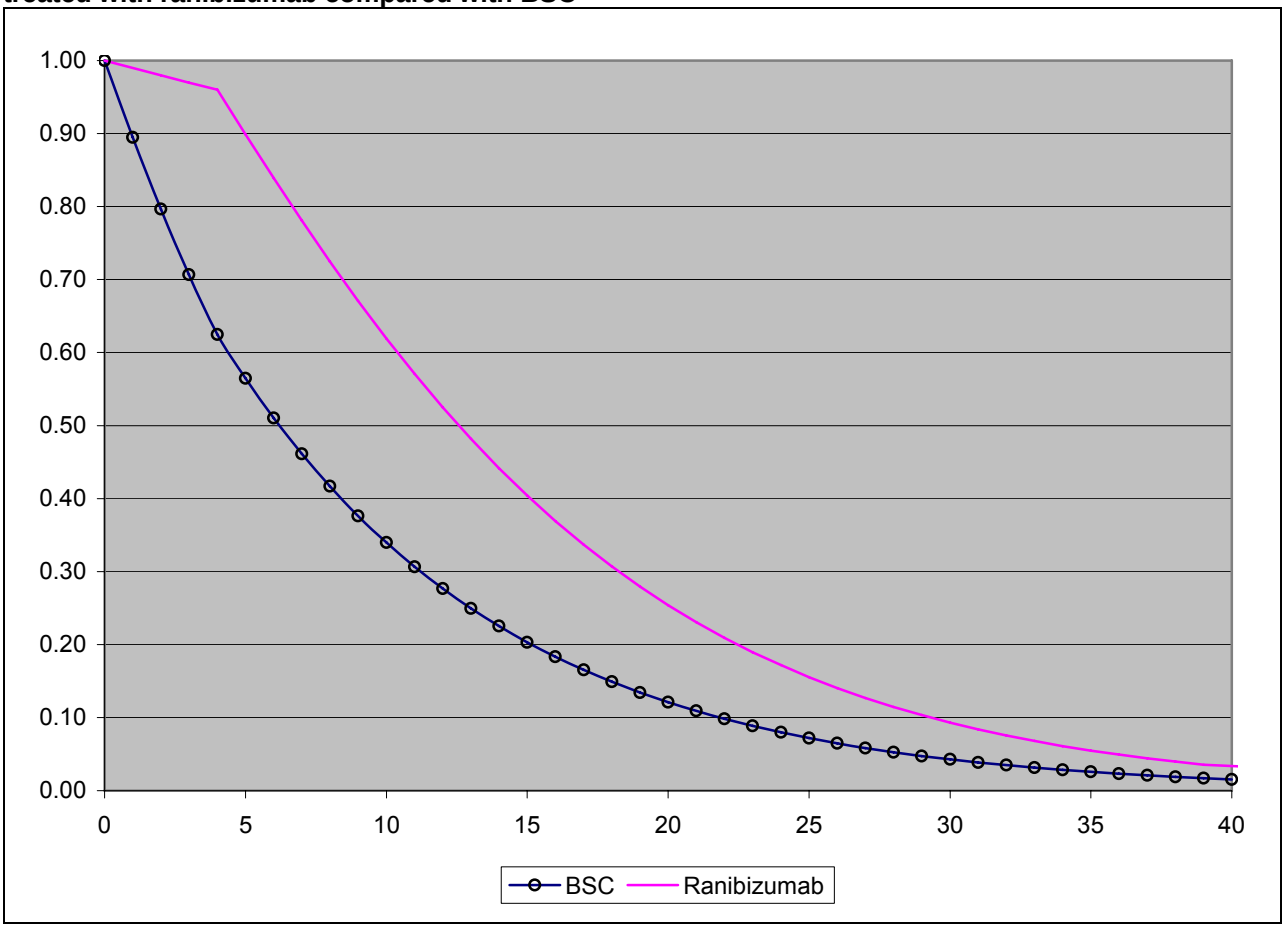
Predominantly classic lesions treated with ranibizumab, compared with PDT.

Figure 5: proportion of cohort surviving and sighted over 10 years, predominantly classic lesions treated with ranibizumab compared with PDT



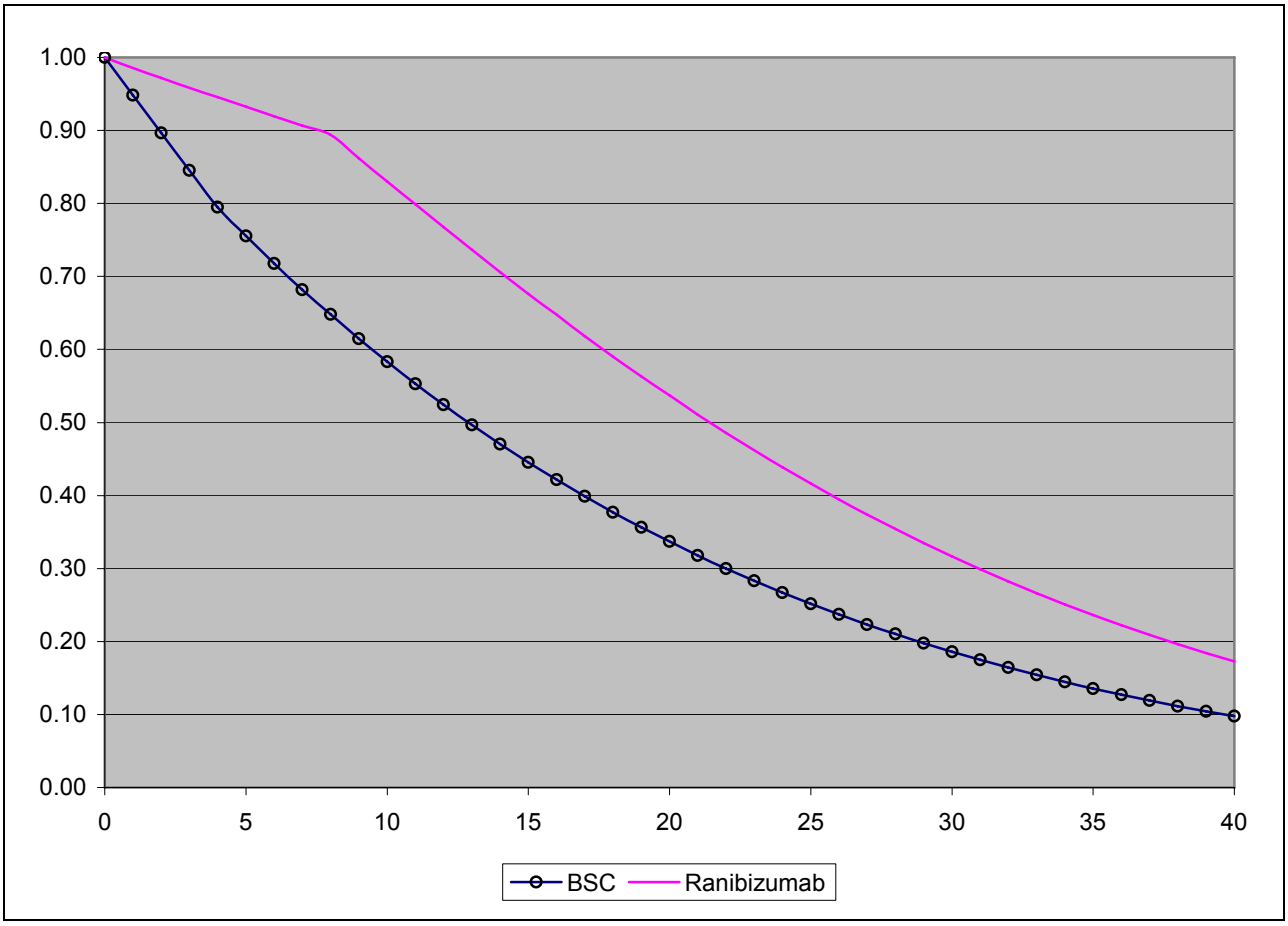
Predominantly classic lesions treated with ranibizumab, compared with BSC.

Figure 6: proportion of cohort surviving and sighted over 10 years, predominantly classic lesions treated with ranibizumab compared with BSC



Minimally classic and occult no classic lesions treated with ranibizumab

Figure 7: proportion of cohort surviving and sighted over 10 years, minimally classic and occult no classic lesions treated with ranibizumab



Extend ranibizumab treatment of predominantly classic lesions to two years

The approach to this involves assuming that treatment beyond the first year will maintain stabilisation of VA, but will not lead to further significant improvements. Transition probabilities for year 1 are based on the proportions improving or losing vision shown in column 2 of

Table 46 below. For year 2 transition probabilities for deterioration of vision are based on the proportions losing vision in column 2, with the probability of gaining vision reverting to the value applied in the BSC cohort, derived from the TAP study PC population.

Table 46: values used to extrapolate to two years treatment with Lucentis (PC)

	Year 1	Year 2
Gaining greater than 3 lines	36.69%	4.53%
Losing 3 to 6 lines	2.16%	2.16%
Losing greater than 6 lines	0.00%	0.00%

Predominantly classic lesions treated with ranibizumab for second year, compared with PDT.

Incremental effectiveness increases from 0.34 QALYs to 0.56 QALYs in this scenario. Incremental cost becomes £11,975 and the ICER at base case assumptions (i.e. 12 injections per year of treatment) is £21,241, see Table 47.

Table 47: results for second year of treatment with ranibizumab for predominantly classic lesions compared with PCT

	Costs (£)	QALYs	ICER
PDT	23,455	3.89	
Ranibizumab	35,430	4.45	21,241

Table 48 shows the breakdown of the total costs (reported in Table 47). Clearly drug and monitoring costs (for ranibizumab) have approximately doubled by adding an extra year of treatment. At the same time the costs of blindness for ranibizumab have reduced by approximately 20%.

Table 48: breakdown of total costs for each cohort by major categories. Using assessment group unit costs

		Drug	Admin and Monitoring	Adverse events	PDT	Blindness
	PDT	0	0	148	7,041	16,266
	Ran	17,330	6,281	220	0	11,598

Table 49 reports a sensitivity analysis, assuming equal effectiveness, for the reduced frequency dosing regime: firstly that reported in the assessment report of 9 injections per year and secondly based on results reported in consultation (based on PRONTO study).

Table 49: sensitivity analysis on number of injections (corrected analysis) for two years of treatment with ranibizumab for predominantly classic lesions compared with PCT

Strategy	Incremental cost (£)	Incremental QALYs	ICER (£)
Base case	11,975	0.56	21,241
9 injections yr 1, 9 yr 2	7,129	0.56	12,645
9 injections yr 1, 6 yr 2	4,798	0.56	8,511
5.6 injections yr 1, 5.6 yr 2‡	1,636	0.56	2,903

Notes: ‡ as reported for year 1 in PRONTO publication{19}

Predominantly classic lesions treated with ranibizumab for second year, compared with BSC.

Incremental effectiveness increases from 0.57 QALYs to 0.94 QALYs in this scenario. Incremental cost becomes £14,467 and the ICER at base case assumptions (i.e. 12 injections per year of treatment) is £15,382, see Table 50.

Table 50: results for second year of treatment with ranibizumab for predominantly classic lesions compared with BSC

	Costs (£)	QALYs	ICER
PDT	20,963	3.51	
Ranibizumab	35,430	4.45	15,382

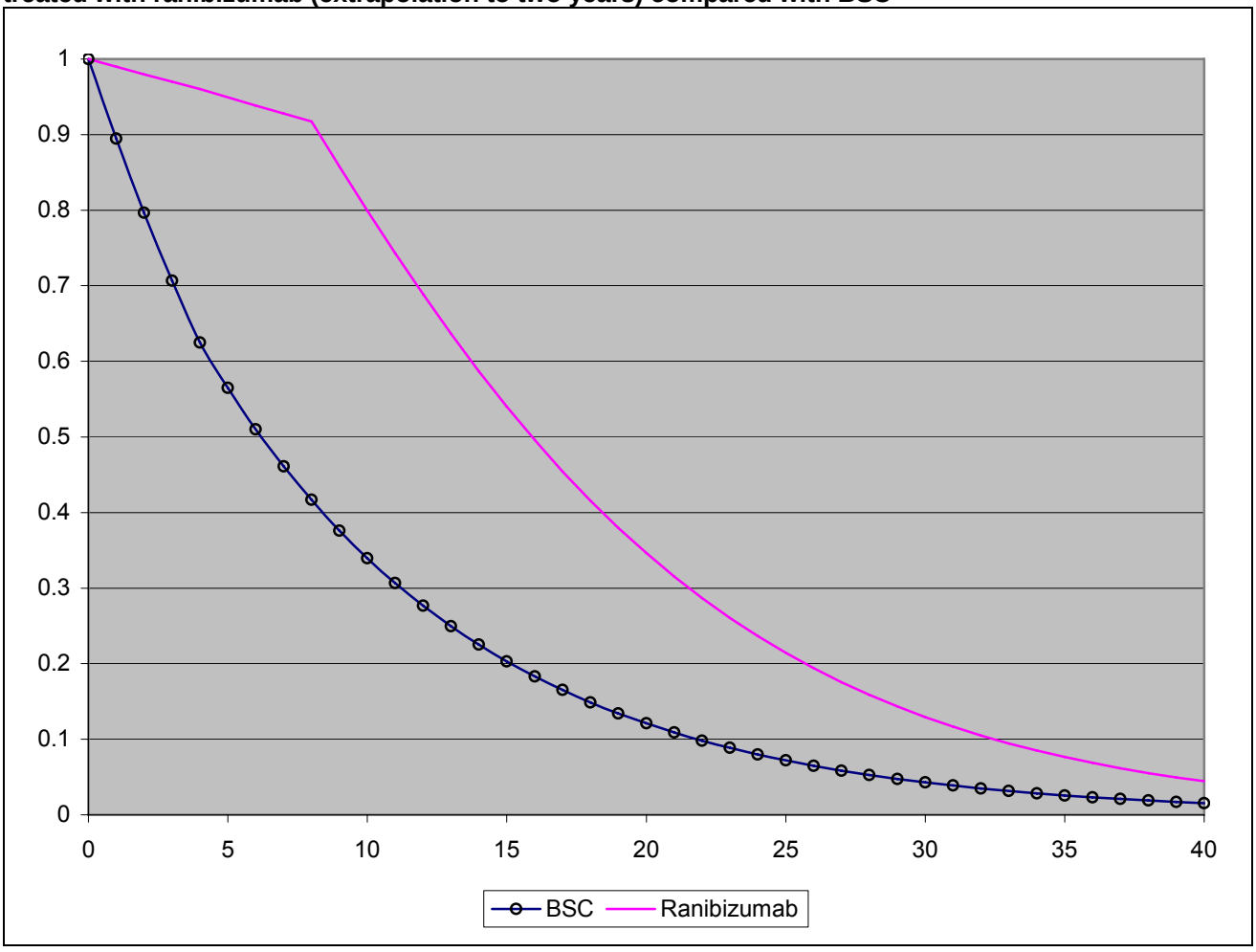
Table 51 reports a sensitivity analysis, assuming equal effectiveness, for the reduced frequency dosing regime: firstly that reported in the assessment report of 9 injections per year and secondly based on results reported in consultation (based on PRONTO study).

Table 51: Sensitivity analysis on number of injections (corrected analysis)

Strategy	Incremental cost (£)	Incremental QALYs	ICER (£)
Base case	14,467	0.94	15,382
9 injections yr 1, 9 yr 2	9,621	0.94	10,230
9 injections yr 1, 6 yr 2	7,291	0.94	7,752
5.6 injections yr 1, 5.6 yr 2‡	4,129	0.94	4,390
Notes: ‡ as reported for year 1 in PRONTO publication{19}			

Graphical presentation of vision survival for predominantly classic lesions treated with ranibizumab for two years, compared with BSC.

Figure 8: proportion of cohort surviving and sighted over 10 years, predominantly classic lesions treated with ranibizumab (extrapolation to two years) compared with BSC



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Appendix A – Cost of blindness in assessment report. Background

We have also included tables illustrating this breakdown of costs for the costs of blindness scenarios reported in the deterministic sensitivity analyses.

Pegaptanib-treated cohort compared with usual care

Costs of blindness for the cohort treated with pegaptanib or receiving usual care are given in the assessment report (Table 4.23) as £12,666 and £15,789 respectively. These are broken down into costs that are assumed to be one-off costs of the transition to blindness (blind registration, provision of low vision aids and low vision rehabilitation) and costs that occur in each year of blindness (community care, residential care, treatment for depression and treatment of fractures following accidents). Table 52 reports the recurring costs of blindness and their proportion of the total estimated costs of blindness. It can be readily seen that, under the assumptions adopted in the assessment report, these recurring costs constitute the vast majority of the costs of blindness (99%) with residential care costs constituting the major portion of these costs.

Table 52: proportion of costs of blindness by type (recurring costs)

	Community Care	Residential Care	Depression	Fractures	Total
Pegaptanib	1,005 (7.9)	10,411 (82.2)	429 (3.4)	688 (5.4)	12,533
Usual care	1,254 (7.9)	12,995 (82.3)	536 (3.4)	858 (5.4)	15,643

Table 53 reports the one-off costs of blindness – it is clear that these are the minority of costs, under the assumptions adopted in the assessment report. One adjustment to this would be to require some additional (updating) of low vision aids or low vision rehabilitation (included in a sensitivity analysis later).

Table 53: proportion of costs of blindness by type (one-off costs)

	Blind registration	Low vision aids	Low vision rehabilitation	Total
Pegaptanib	77 (0.6)	36 (0.3)	20 (0.2)	133
Usual care	85 (0.5)	39 (0.2)	22 (0.1)	146

Table 54 reports the recurring costs of blindness and their proportion of the total estimated costs of blindness in the scenarios reported in the sensitivity analyses in Table 4.24 (page 135) of the assessment report.

Table 54: proportion of costs of blindness by type in sensitivity analyses (recurring costs)

		Community Care	Residential Care	Depression	Fractures	Total
High uptake	Pegaptanib	6,700 (14.5)	34,337 (74.4)	552 (1.2)	4,348 (9.4)	45,937
High cost	Usual care	8,362 (14.5)	42,858 (74.4)	689 (1.2)	5,427 (9.4)	57,337
Low uptake	Pegaptanib	240 (9.4)	2,160 (84.8)	66 (2.6)	43 (1.7)	2,510
Low cost	Usual care	300 (9.4)	2,696 (84.9)	83 (2.6)	54 (1.7)	3,133

Medium uptake	Pegaptanib	1,005 (4.8)	18,394 (88.1)	429 (2.1)	879 (4.2)	20,707
High cost	Usual care	1,254 (4.8)	22,959 (88.2)	536 (2.1)	1,098 (4.2)	25,846
Medium uptake	Pegaptanib	240 (3.9)	4,985 (81.1)	429 (7.0)	445 (7.2)	6,099
Low cost	Usual care	300 (3.9)	6,222 (81.1)	536 (7.0)	555 (7.2)	7,613
High uptake	Pegaptanib	6,700 (22.1)	19,435 (64.2)	552 (1.8)	3,397 (11.2)	30,083
Medium cost	Usual care	8,362 (22.2)	24,258 (64.3)	689 (1.8)	4,240 (11.2)	37,549
Low uptake	Pegaptanib	1,005 (17.5)	4,512 (78.5)	66 (1.2)	69 (1.2)	5,652
Medium cost	Usual care	1,254 (17.5)	5,631 (78.6)	83 (1.2)	86 (1.2)	7,054

Table 55 reports the one-off costs of blindness and their proportion of the total estimated costs of blindness in the scenarios reported in the sensitivity analyses in Table 4.24 (page 135) of the assessment report.

Table 55: proportion of costs of blindness by type in sensitivity analyses (one-off costs)

		Blind registration	Low vision aids	Low vision rehabilitation	Total
High uptake	Pegaptanib	114 (0.2)	79 (0.2)	24 (0.1)	217
High cost	Usual care	125 (0.2)	87 (0.2)	27 (0.0)	238
Low uptake	Pegaptanib	14 (0.6)	14 (0.5)	10 (0.4)	38
Low cost	Usual care	16 (0.5)	15 (0.5)	11 (0.3)	41
Medium uptake	Pegaptanib	114 (0.5)	36 (0.2)	24 (0.1)	173
High cost	Usual care	125 (0.5)	39 (0.1)	27 (0.1)	190
Medium uptake	Pegaptanib	27 (0.4)	14 (0.2)	10 (0.2)	50
Low cost	Usual care	30 (0.4)	15 (0.2)	11 (0.1)	55
High uptake	Pegaptanib	77 (0.3)	79 (0.3)	20 (0.1)	176
Medium cost	Usual care	85 (0.2)	87 (0.2)	22 (0.1)	193
Low uptake	Pegaptanib	41 (0.7)	36 (0.6)	20 (0.3)	97
Medium cost	Usual care	45 (0.6)	39 (0.5)	22 (0.3)	106

Predominantly classic lesions treated for one year, compared with PDT.

Costs of blindness for cohort with predominantly classic lesions treated with ranibizumab or PDT are given in the assessment report (Table 4.28) as £14,461 and £17,575 respectively. These are broken down into costs that are assumed to be one-off costs of the transition to blindness (blind registration, provision of low vision aids and low vision rehabilitation) and costs that occur in each year of blindness (community care, residential care, treatment for depression and treatment of fractures following accidents). Table 56 reports the recurring costs of blindness and their proportion of the total estimated costs of blindness. It can be readily seen that, under the assumptions adopted in the assessment report, these recurring costs constitute the vast majority of the costs of blindness (99%) with residential care costs constituting the major portion of these costs.

Table 56: proportion of costs of blindness by type (recurring costs)

	Community Care	Residential Care	Depression	Fractures	Total

Ranibizumab	1,147 (7.9)	11,890 (82.2)	490 (3.4)	785 (5.4)	14,313
PDT	1,396 (7.9)	14,466 (82.3)	597 (3.4)	955 (5.4)	17,414

Table 57 reports the one-off costs of blindness – it is clear that these are the minority of costs, under the assumptions adopted in the assessment report. One adjustment to this would be to require some additional (updating) of low vision aids or low vision rehabilitation (included in a sensitivity analysis later).

Table 57: proportion of costs of blindness by type (one-off costs)

	Blind registration	Low vision aids	Low vision rehabilitation	Total
Ranibizumab	86 (0.6)	40 (0.3)	22 (0.2)	148
PDT	94 (0.5)	43 (0.2)	24 (0.1)	161

Table 58 reports the recurring costs of blindness and their proportion of the total estimated costs of blindness in the scenarios reported in the sensitivity analyses in Table 4.29 (page 145) of the assessment report.

Table 58: proportion of costs of blindness by type in sensitivity analyses (recurring costs)

		Community Care	Residential Care	Depression	Fractures	Total
High uptake	Ranibizumab	7,651 (15.2)	39,214 (78.0)	631 (1.3)	2,511 (5.0)	50,006
High cost	PDT	9,309 (15.2)	47,709 (78.1)	767 (1.3)	3,054 (5.0)	60,840
Low uptake	Ranibizumab	274 (9.3)	2,467 (83.4)	76 (2.6)	99 (3.4)	2,916
Low cost	PDT	334 (9.3)	3,001 (83.5)	92 (2.6)	121 (3.4)	3,548
Medium uptake	Ranibizumab	1,147 (4.9)	21,007 (90.0)	490 (2.1)	508 (2.2)	23,152
High cost	PDT	1,396 (4.9)	25,558 (90.1)	597 (2.1)	618 (2.2)	28,168
Medium uptake	Ranibizumab	274 (3.7)	5,692 (75.7)	490 (6.5)	1,004 (13.4)	7,461
Low cost	PDT	334 (3.7)	6,926 (75.8)	597 (6.5)	1,222 (13.4)	9,078
High uptake	Ranibizumab	7,651 (22.1)	22,195 (64.2)	631 (1.8)	3,880 (11.2)	34,356
Medium cost	PDT	9,309 (22.2)	27,003 (64.3)	767 (1.8)	4,720 (11.2)	41,799
Low uptake	Ranibizumab	1,147 (17.5)	5,152 (78.5)	76 (1.2)	79 (1.2)	6,454
Medium cost	PDT	1,396 (17.5)	6,269 (78.7)	92 (1.2)	96 (1.2)	7,853

Table 59 reports the one-off costs of blindness and their proportion of the total estimated costs of blindness in the scenarios reported in the sensitivity analyses in Table 4.29 (page 145) of the assessment report.

Table 59: proportion of costs of blindness by type in sensitivity analyses (one-off costs)

		Blind registration	Low vision aids	Low vision rehabilitation	Total
High uptake	Ranibizumab	127 (0.3)	88 (0.2)	27 (0.1)	242
High cost	PDT	138 (0.2)	96 (0.2)	29 (0.0)	263
Low uptake	Ranibizumab	16 (0.5)	15 (0.5)	11 (0.4)	42
Low cost	PDT	17 (0.5)	16 (0.5)	12 (0.3)	46

Medium uptake	Ranibizumab	127 (0.5)	40 (0.2)	27 (0.1)	194
High cost	PDT	138 (0.5)	43 (0.2)	29 (0.1)	210
Medium uptake	Ranibizumab	30 (0.4)	15 (0.2)	11 (0.1)	56
Low cost	PDT	33 (0.4)	16 (0.2)	12 (0.1)	61
High uptake	Ranibizumab	86 (0.3)	88 (0.3)	22 (0.1)	197
Medium cost	PDT	94 (0.2)	96 (0.2)	24 (0.1)	213
Low uptake	Ranibizumab	46 (0.7)	40 (0.6)	22 (0.3)	108
Medium cost	PDT	50 (0.6)	43 (0.5)	24 (0.3)	117

Predominantly classic lesions treated for one year, compared with BSC.

Costs of blindness for cohort with predominantly classic lesions treated with ranibizumab or BSC are given in the assessment report (Table 4.28) as £20,210 and £14,461 respectively. Table 60 reports the recurring costs of blindness and their proportion of the total estimated costs of blindness. It can be readily seen that, under the assumptions adopted in the assessment report, these recurring constitute the vast majority of the costs of blindness (99%) with residential care costs constituting the major portion of these costs.

Table 60: proportion of costs of blindness by type

	Community Care	Residential Care	Depression	Fractures	Total
Ranibizumab	1,147 (7.9)	11,890 (82.2)	490 (3.4)	785 (5.4)	14,313
BSC	1,606 (7.9)	16,648 (82.4)	687 (3.4)	1,100 (5.4)	20,041

Table 61 reports the one-off costs of blindness – it is clear that these are the minority of costs, under the assumptions adopted in the assessment report. One adjustment to this would be to require some additional (updating) of low vision aids or low vision rehabilitation (included in a sensitivity analysis later).

Table 61: proportion of costs of blindness by type

	Blind registration	Low vision aids	Low vision rehabilitation	Total
Ranibizumab	86 (0.6)	40 (0.3)	22 (0.2)	148
BSC	99 (0.5)	45 (0.2)	25 (0.1)	169

Table 62 reports the recurring costs of blindness and their proportion of the total estimated costs of blindness in the scenarios reported in the sensitivity analyses in Table 4.30 (page 146) of the assessment report.

Table 62: proportion of costs of blindness by type in sensitivity analyses (recurring costs)

		Community Care	Residential Care	Depression	Fractures	Total
High uptake	Ranibizumab	7,651 (15.2)	39,214 (78.0)	631 (1.3)	2,511 (5.0)	50,006
High cost	PDT	10,713 (15.2)	54,907 (78.1)	883 (1.3)	3,515 (5.0)	70,019
Low uptake	Ranibizumab	274 (9.3)	2,467 (83.4)	76 (2.6)	99 (3.4)	2,916

Low cost	PDT	384 (9.3)	3,454 (83.6)	106 (2.6)	139 (3.4)	4,083
Medium uptake	Ranibizumab	1,147 (4.9)	21,007 (90.0)	490 (2.1)	508 (2.2)	23,152
High cost	PDT	1,606 (4.9)	29,414 (90.1)	687 (2.1)	711 (2.2)	32,418
Medium uptake	Ranibizumab	274 (3.7)	5,692 (75.7)	490 (6.5)	1,004 (13.4)	7,461
Low cost	PDT	384 (3.7)	7,971 (75.8)	687 (6.5)	1,406 (13.4)	10,448
High uptake	Ranibizumab	7,651 (22.1)	22,195 (64.2)	631 (1.8)	3,880 (11.2)	34,356
Medium cost	PDT	10,713 (22.2)	31,077 (64.3)	883 (1.8)	5,432 (11.2)	48,106
Low uptake	Ranibizumab	1,147 (17.5)	5,152 (78.5)	76 (1.2)	79 (1.2)	6,454
Medium cost	PDT	1,606 (17.5)	7,214 (78.8)	106 (1.2)	110 (1.2)	9,037

Table 63 reports the one-off costs of blindness and their proportion of the total estimated costs of blindness in the scenarios reported in the sensitivity analyses in Table 4.30 (page 146) of the assessment report.

Table 63: proportion of costs of blindness by type in sensitivity analyses (one-off costs)

		Blind registration	Low vision aids	Low vision rehabilitation	Total
High uptake	Ranibizumab	127 (0.3)	88 (0.2)	27 (0.1)	242
High cost	PDT	145 (0.2)	101 (0.1)	31 (0.0)	276
Low uptake	Ranibizumab	16 (0.5)	15 (0.5)	11 (0.4)	42
Low cost	PDT	18 (0.4)	17 (0.4)	13 (0.3)	48
Medium uptake	Ranibizumab	127 (0.5)	40 (0.2)	27 (0.1)	194
High cost	PDT	145 (0.4)	45 (0.1)	31 (0.1)	221
Medium uptake	Ranibizumab	30 (0.4)	15 (0.2)	11 (0.1)	56
Low cost	PDT	34 (0.3)	17 (0.2)	13 (0.1)	64
High uptake	Ranibizumab	86 (0.3)	88 (0.3)	22 (0.1)	197
Medium cost	PDT	99 (0.2)	101 (0.2)	25 (0.1)	225
Low uptake	Ranibizumab	46 (0.7)	40 (0.6)	22 (0.3)	108
Medium cost	PDT	53 (0.6)	45 (0.5)	25 (0.3)	123

Minimally classic and occult no classic treated for two years

Costs of blindness for cohort with predominantly classic lesions treated with ranibizumab or BSC are given in the assessment report (Table 4.28) as £13,567 and £7,313 respectively. Table 64 reports the recurring costs of blindness and their proportion of the total estimated costs of blindness. It can be readily seen that, under the assumptions adopted in the assessment report, these recurring constitute the vast majority of the costs of blindness (99%) with residential care costs constituting the major portion of these costs.

Table 64: proportion of costs of blindness by type

	Community Care	Residential Care	Depression	Fractures	Total
Ranibizumab	578 (7.9)	5,995 (82.0)	247 (3.4)	396 (5.4)	7,217
BSC	1,077 (7.9)	11,160 (82.3)	460 (3.4)	737 (5.4)	13,434

Table 65 reports the one-off costs of blindness – it is clear that these are the minority of costs, under the assumptions adopted in the assessment report. One adjustment to this would be to require some additional (updating) of low vision aids or low vision rehabilitation (included in a sensitivity analysis later).

Table 65: proportion of costs of blindness by type

	Blind registration	Low vision aids	Low vision rehabilitation	Total
Ranibizumab	56 (0.8)	26 (0.4)	14 (0.2)	96
BSC	77 (0.6)	35 (0.3)	20 (0.1)	133

Table 66 reports the recurring costs of blindness and their proportion of the total estimated costs of blindness in the scenarios reported in the sensitivity analyses in Table 4.31 (page 147) of the assessment report.

Table 66: proportion of costs of blindness by type in sensitivity analyses (recurring costs)

		Community Care	Residential Care	Depression	Fractures	Total
High uptake	Ranibizumab	3,858 (15.2)	19,773 (77.9)	318 (1.3)	1,266 (5.0)	25,215
High cost	PDT	7,181 (15.2)	36,806 (78.1)	592 (1.3)	2,356 (5.0)	46,936
Low uptake	Ranibizumab	138 (9.2)	1,244 (83.0)	38 (2.6)	50 (3.3)	1,470
Low cost	PDT	258 (9.3)	2,315 (83.4)	71 (2.6)	93 (3.4)	2,737
Medium uptake	Ranibizumab	578 (4.9)	10,592 (89.8)	247 (2.1)	256 (2.2)	11,674
High cost	PDT	1,077 (4.9)	19,717 (90.0)	460 (2.1)	477 (2.2)	21,731
Medium uptake	Ranibizumab	138 (3.6)	2,870 (75.6)	247 (6.5)	506 (13.3)	3,762
Low cost	PDT	258 (3.7)	5,343 (75.7)	460 (6.5)	943 (13.4)	7,003
High uptake	Ranibizumab	3,858 (22.1)	11,191 (64.1)	318 (1.8)	1,956 (11.2)	17,323
Medium cost	PDT	7,181 (22.1)	20,832 (64.3)	592 (1.8)	3,641 (11.2)	32,247
Low uptake	Ranibizumab	578 (17.4)	2,598 (78.2)	38 (1.2)	40 (1.2)	3,254
Medium cost	PDT	1,077 (17.5)	4,836 (78.6)	71 (1.2)	74 (1.2)	6,058

Table 67 reports the one-off costs of blindness and their proportion of the total estimated costs of blindness in the scenarios reported in the sensitivity analyses in Table 4.31 (page 147) of the assessment report.

Table 67: proportion of costs of blindness by type in sensitivity analyses (one-off costs)

		Blind registration	Low vision aids	Low vision rehabilitation	Total
High uptake	Ranibizumab	82 (0.3)	57 (0.2)	17 (0.1)	157
High cost	PDT	113 (0.2)	79 (0.2)	24 (0.1)	216
Low uptake	Ranibizumab	10 (0.7)	10 (0.7)	7 (0.5)	27
Low cost	PDT	14 (0.5)	13 (0.5)	10 (0.4)	38
Medium uptake	Ranibizumab	82 (0.7)	26 (0.2)	17 (0.1)	125
High cost	PDT	113 (0.5)	35 (0.2)	24 (0.1)	173
Medium uptake	Ranibizumab	20 (0.5)	10 (0.3)	7 (0.2)	36

Low cost	PDT	27	(0.4)	13	(0.2)	10	(0.1)	50
High uptake	Ranibizumab	56	(0.3)	57	(0.3)	14	(0.1)	127
Medium cost	PDT	77	(0.2)	79	(0.2)	20	(0.1)	176
Low uptake	Ranibizumab	30	(0.9)	26	(0.8)	14	(0.4)	70
Medium cost	PDT	41	(0.7)	35	(0.6)	20	(0.3)	96

Appendix B

VA range	Mean TTO	95% CI
≥20/50	0.864	0.814 to 0.914
20/60 to 20/100	0.783	0.735 to 0.832
20/125 to 20/160	0.688	0.601 to 0.776
20/200 to 20/400	0.635	0.544 to 0.727
<20/400	0.497	0.416 to 0.577

A visual acuity of ≥20/50 implies an ability to read 65 letters or more – assume an upper limit to this range at 20/10, where number of letters read us 100 – giving a median for this VA range of 82.5 letters. Similar median values were estimated for the other visual acuity ranges. A simple linear regression model was estimated to predict mean TTO valuations for the visual acuity ranges used in the assessment group model – the estimated values are shown in Table 68.

Table 68: estimated utilities for assessment group model

VA range	Utility - estimated
≥6/12	0.900
≤6/12 to >6/24	0.786
≤6/24 to >6/60	0.697
≤6/60 to >3/60	0.609
≤3/60	0.518