VALUE BASED OPHTHALMOLOGY

Cost effectiveness of photodynamic therapy with verteporfin for age related macular degeneration: the UK case

D H Smith, P Fenn, M Drummond

Br J Ophthalmol 2004;**88**:1107–1112. doi: 10.1136/bjo.2003.023986

Series editors: Melissa and Gary Brown

See end of article for authors' affiliations

Correspondence to: David H Smith, Center for Health Research, Kaiser Permanente Northwest, 3800 N Interstate Ave, Portland, OR 97211, USA; David.Smith@kpchr.org

Accepted for publication 27 November 2003

Aim: To estimate the potential cost effectiveness of photodynamic therapy (PDT) with verteporfin in the UK setting.

Methods: Using data from a variety of sources a Markov model was built to produce estimates of the cost effectiveness (incremental cost per quality adjusted life year (QALY) and incremental cost per vision year gained) of PDT for two cohorts of patients (one with starting visual acuity (VA) of 20/40 and one at 20/100) with predominantly classic choroidal neovascular disease over a 2 year and 5 year time horizon. A government perspective and a treatment cost only perspective were considered. Probabilistic and one way sensitivity analyses were undertaken.

Results: From the government perspective, over the 2 year period, the expected incremental cost effectiveness ratios range from £286 000 (starting VA 20/100) to £76 000 (starting VA 20/40) per QALY gained and from £14 000 (20/100) to £34 000 (20/40) per vision year gained. A 5 year perspective yields incremental ratios less than £5000 for vision years gained and from £9000 (20/40) to £30 000 (20/100) for QALYs gained. Without societal or NHS cost offsets included, the 2 year incremental cost per vision year gained ranges from £20 000 (20/100) to £40 000 (20/40), and the 2 year incremental cost per QALY gained ranges from £412 000 (20/100) to £90 000 (20/40). The 5 year time frame shows expected costs of £7000 (20/40) to £10 000 (20/100) per vision year gained and from £38 000 (20/40) to £69 000 (20/100) per QALY gained.

Conclusion: This evaluation suggests that early treatment (that is, treating eyes at less severe stages of disease) with PDT leads to increased efficiency. When considering only the cost of therapy, treating people at lower levels of visual acuity would probably not be considered cost effective. However, a broad perspective that incorporates other NHS treatment costs and social care costs suggests that over a long period of time, PDT may yield reasonable value for money.

Age related macular degeneration (AMD) is the leading cause of registered blindness in the United Kingdom,[1] has prevalence of >7% in the elderly,[2] and is the main cause of severe and irreversible loss of vision in developed countries,[3] leading to quality of life decrements.[4] The wet form of AMD is characterised by choroidal neovascularisation (CNV) and may lead to acute visual loss.

Until recently, the only available treatment for wet AMD was laser photocoagulation, but in the case of those with subfoveal lesions (about 50%), it leads to immediate loss of vision.[3]

This study examined the cost effectiveness in the United Kingdom of photodynamic therapy (PDT) with verteporfin, a treatment shown to slow the vision loss associated with subfoveal CNV.[5] Unlike previous analyses,[6 7] our study is both long term and UK specific.

CLINICAL DATA

We obtained patient level data from the Treatment of AMD with PDT (TAP) clinical trial.[5] The TAP trial included 609 patients presenting with AMD subfoveal CNV lesions having a greatest linear dimension of ⩽5400 μm, some evidence of classic CNV, and best corrected visual acuity between 20/40 and 20/200. One eye from each patient was randomised, 402 to treatment and 207 to placebo. At each 3 month follow up visit, patients were retreated with the baseline regimen if fluorescein leakage from CNV was identified on angiography.

The primary study outcome was moderate vision loss (of the enrolled eye), defined as loss of less than three lines of visual acuity (15 letters). Of those patients treated with verteporfin, 53% lost less than three lines of vision compared to 38% of placebo treated eyes ($p<0.001$). A total of 82% of those on verteporfin and 70% on placebo ($p<0.001$) did not experience severe vision loss (defined as a loss of less than six lines, or less than 30 letters).

Prospectively planned subgroup analysis showed similar visual outcomes (loss of less than 15 letters at 24 months) for placebo and PDT in patients with minimally classic lesions (48% for verteporfin patients versus 44% of the placebo patients), but patients with predominantly classic lesions given PDT had lower vision loss (59% of those on verteporfin versus 31% of those on placebo).

Since the approved labelling and current recommendation for use of verteporfin in the United Kingdom indicate that only those with predominantly classic CNV should be treated, this analysis focuses on the subset of 243 patients with that particular form of disease.

MODELLING THE BENEFITS OF PDT WITH VERTEPORFIN

We used a Markov model to estimate cost effectiveness for two time periods—2 years (equivalent to a within trial estimate) and 5 years. Five years represents a time frame over which decision making bodies might project and

Abbreviations: AMD, age related macular degeneration; CNV, choroidal neovascularisation; PDT, photodynamic therapy; QALY, quality adjusted life year; VA, visual acuity

minimises the assumptions associated with lengthier extrapolation. The health states used in the Markov model came directly from clinical trial visual acuity measurements and ranged from 20/40 to worse than 20/800, plus the dead state. Survival analysis with a Weibull function estimated daily transition probabilities of moving to a lower state of visual acuity, controlling for baseline visual acuity, sex, and age. Since there were 15 levels of visual acuity possible in the trial, a person starting at the best level of acuity would need to experience 14 Snellen ''drops'' to reach the worst level of acuity in the trial. The predicted hazard was then used to calculate the probability of progression for verteporfin and placebo, and the uncertainty estimates were used to estimate the distribution in our probabilistic sensitivity analysis. The survival function from this hazard can be written as:

$$\exp(-(\lambda t)^{\alpha})$$

where λ is the Weibull scale parameter, modelled as a log linear function of the regressors (that is, $\lambda = \exp(-\beta x)$), and α is the Weibull shape parameter, which determines whether the hazard increases or decreases with time. The time component (t) was varied to produce daily estimates of the transition probability to a lower level of visual acuity.

Visual acuity was measured every 3 months in the trial, so linear interpolation estimated the day when a person dropped more than one line of vision between 3 month clinic visits.

Data Pro (release 6) was used to build the Markov model; we incorporated probability distributions to generate cost effectiveness acceptability curves. This model is based on a cohort of men aged 75 years at the start of therapy.

OUTCOME MEASURES

Vision years were calculated based on time spent with visual acuity of 20/200 or better, as has been used in previous studies; this represents ''legal blindness'' in many countries, including the United Kingdom.

Health state preference values were taken from a time trade-off study of 80 patients with AMD.[6] These utilities were 20/20–20/25, 0.89 (95% CI, 0.82 to 0.96), 20/30–20/50, 0.81 (95% CI, 0.73 to 0.89), 20/60–20/100, 0.57 (95% CI, 0.47 to 0.67), 20/200–20/400, 0.52 (95% CI, 0.38 to 0.66), and the ability to count fingers to light perception, 0.40 (95% CI, 0.29 to 0.50). The uncertainty in the utility estimates was incorporated into the probabilistic sensitivity analysis.

All side effects, with the exception of allergic reactions, were more prominent in the verteporfin arm.[5] We incorporated the effect of these adverse events through changes in quality of life, using values from a previous cost effectiveness analysis on PDT.[8] To the extent that these adverse events cause decreases in vision, their costs are included. We considered costs of other adverse events to be trivial.

Costs and benefits were discounted at a rate of 6% for costs and 2% for benefits following recommendations from the UK Treasury.[9]

MODEL CALIBRATION

The model predicts gains in vision years based on baseline visual acuity level. To compare the model predictions to the actual data, we used an average of the model predictions, weighted by the proportion of people in the trial at each visual acuity level; transition to the death state was not allowed, and the results were undiscounted. The clinical trial showed a vision year gain of about 0.39 years. The model predicted a gain of 0.34 years over the 2 year period, or 87% of the actual gain. Therefore, the model appears to produce conservative but comparable estimates to the clinical trial.[10]

COSTS

We present cost estimates from two perspectives, one considering only the NHS treatment costs (treatment cost only), and one similar to the National Institute for Clinical Excellence's (NICE) recommendation that NHS and personal social services costs should be considered (government perspective). The cost estimates in the model are taken from NICE's technology assessment report on PDT with verteporfin[7] which includes estimates from published national sources (for example, the *British National Formulary*, NHS Reference Costs, Personal Social Services Research Unit Costs of Health and Social Care), primary literature, and some primary data collection. All costs have been inflated to December 2000 prices and reflect the proportion of people who would experience the cost in a given year. The estimate of treatment cost only (£1181) includes the cost of verteporfin and disposables (£860), laser (£101), angiography (£108), and outpatient appointment (£112).

Because PDT with verteporfin may diminish the rate at which individuals become blind (that is,<20/200), the government perspective incorporates possible cost offsets in medical and social care. The total base case government cost (exclusive of treatment cost) was estimated at £6295 per year (range £1325 to £16 800), plus a one-off cost of £159 (range £50 to £300) for blindness registration, low vision aids, and rehabilitation services. The annual government costs also include housing and council tax benefit (£1221), social security (£1212), tax allowance (£16), depression treatment (£151), hip replacement (£183), community care (£171), and residential care (£3340). Our conservative approach uses the base case (£6295/year) and a sensitivity analysis on the lower limit of the range (£1325/year) for the government perspective.

ASSUMPTIONS IN THE ANALYSIS

Re-treatments

Patient follow up is suggested at 3 month intervals for those receiving PDT with verteporfin treatment. In the clinical trial, all patients in the verteporfin treated group received follow up treatment if there was evidence of CNV leakage on fluorescein angiography. To estimate the number of re-treatments after the trial, we used a linear trend based on 2 year clinical trial data to predict an average of 1.52 re-treatments per person from year 2 to 3 and none thereafter.

Table 1 Survival analysis regression results

Parameter	DF	Estimate	SE	95% CL	χ^2	Pr χ^2
Intercept	1	3.7905	0.3759	3.0536 to 4.5273	101.66	<0.0001
Sex (1 if male)	1	−0.1769	0.1838	−0.5372 to 0.1834	0.93	0.336
Baseline Snellen*	1	0.1184	0.0435	0.0331 to 0.2037	7.4	0.0065
Previous treatment (Y/N)	1	−0.13	0.1962	−0.5146 to 0.2547	0.44	0.5078
Treatment group (1 if verteporfin)	1	0.5109	0.1926	0.1334 to 0.8885	7.04	0.008
Scale	1	1.3366	0.0678	1.2101 to 1.4762		
Weibull shape	1	0.7482	0.0379	0.6774 to 0.8264		

*Baseline Snellen follows the categories described in the text. DF = degrees of freedom, CL = confidence limits, Pr = probability.

This correlates well with the 3 year open label extension analysis.[11] Further, we assumed that re-treatment was independent of baseline visual acuity.

Follow up visits

This analysis assumed that once re-treatments were completed there would be no further follow up visits for those in the PDT treatment arm. The costs of follow up angiogram and outpatient visits are the subject of a sensitivity analysis. Routine angiograms and visits not related to PDT treatment are assumed to be used at the same rate in both arms.

Treated eye

A critical assumption in the model is that the better seeing eye is the treated eye. Since AMD is a progressive, bilateral disease, the better seeing eye will normally be the second eye involved.

This issue has generated considerable debate during the time that PDT has been subject to appraisal by NICE. Visual function and quality of vision are more strongly correlated with visual acuity in the better seeing eye than in the poorer seeing eye,[12] suggesting that quality of life is more dependent on the better seeing eye. Given the budgetary impact of the widespread use of PDT, this analysis considers a scenario based on treatment of the better seeing eye.

Treatment alternative

In the 12 month results from TAP, 92% of the patients eligible for PDT with verteporfin therapy would not have been eligible for treatment with laser photocoagulation, since they had subfoveal CNV.[13] The proposed guidelines for clinical use of PDT suggest treatment of a similar patient population.

Improvements in vision

Even though the clinical trial showed some improvement in visual acuity associated with verteporfin treatment, the Markov process used here conservatively did not allow for improvement in vision. People stayed at their given level of acuity until their visual acuity worsened. Mortality data for the model were based on the UK population death rates.

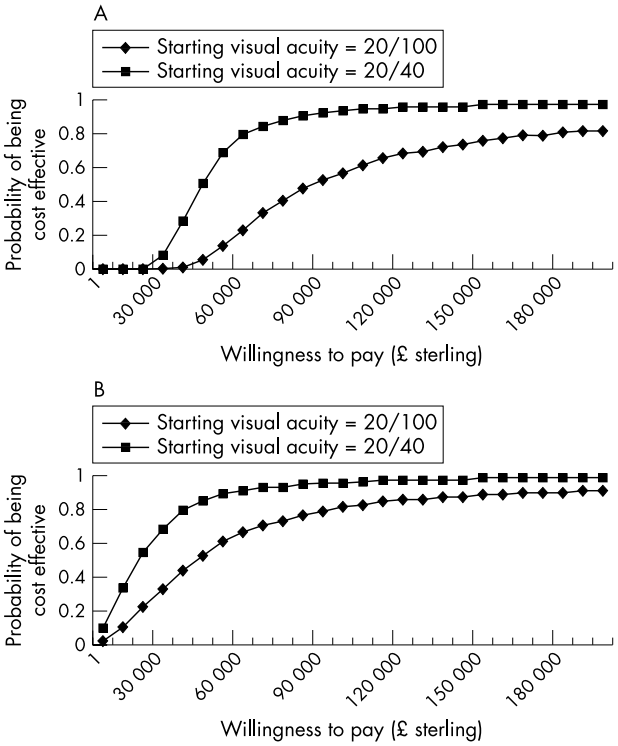

Figure 1 Cost effectiveness acceptability curve on cost per QALY. (A) Treatment cost only, (B) governmental perspective.

Sensitivity analysis

Results are shown for cohorts with starting visual acuity of 20/40 or 20/100 (average starting visual acuity in the TAP trial). Results are also shown with and without NHS and

Table 2 Cost effectiveness (CE): government perspective

2 year time frame, cohort with baseline best corrected visual acuity = 20/40				
	Placebo	**Verteporfin**	**Difference**	**CE ratio**
Cost (£ sterling)	1275	6490	5215	
Vision years	1.618	1.773	0.155	33 645
QALYs	1.136	1.205	0.069	75 580
2 year time frame, cohort with baseline best corrected visual acuity = 20/100				
	Placebo	**Verteporfin**	**Difference**	**CE ratio**
Cost (£ sterling)	4590	8878	4288	
Vision years	1.074	1.383	0.309	13 877
QALYs	0.980	0.995	0.015	285 867
5 year time frame, cohort with baseline best corrected visual acuity = 20/40				
	Placebo	**Verteporfin**	**Difference**	**CE ratio**
Cost (£ sterling)	10 200	11 700	1500	
Vision years	2.160	3.050	0.890	1685
QALYs	2.205	2.375	0.170	8823
5 year time frame, cohort with baseline best corrected visual acuity = 20/100				
	Placebo	**Verteporfin**	**Difference**	**CE ratio**
Cost (£ sterling)	15,700	18,500	2,800	
Vision years	1.222	1.858	0.636	4,402
QALYs	1.999	2.093	0.094	29,787

Table 3 Cost effectiveness (CE): PDT treatment cost only

	Placebo	Verteporfin	Difference	CE ratio
2 year time frame, cohort with baseline best corrected visual acuity = 20/40				
Cost (£ sterling)	0	6173	6173	
Vision years	1.618	1.773	0.155	39 826
QALYs	1.136	1.205	0.069	89 464
2 year time frame, cohort with baseline best corrected visual acuity = 20/100				
	Placebo	**Verteporfin**	**Difference**	**CE ratio**
Cost (£ sterling)	0	6173	6173	
Vision years	1.074	1.383	0.309	19 977
QALYs	0.980	0.995	0.015	411 533
5 year time frame, cohort with baseline best corrected visual acuity = 20/40				
	Placebo	**Verteporfin**	**Difference**	**CE ratio**
Cost (£ sterling)	0	6475	6475	
Vision years	2.160	3.050	0.890	7275
QALYs	2.205	2.375	0.170	38 088
5 year time frame, cohort with baseline best corrected visual acuity = 20/100				
	Placebo	**Verteporfin**	**Difference**	**CE ratio**
Cost (£ sterling)	0	6475	6475	
Vision years	1.222	1.858	0.636	10 180
QALYs	1.999	2.093	0.094	68 882

social care costs. We reduced cost offsets from the government perspective to the low end of the range, and investigated changing assumptions regarding angiographic follow up of those treated with PDT was investigated. We also undertook a probabilistic sensitivity analysis, displayed as a cost effectiveness acceptability curve, wherein we varied transition probabilities and health state utilities assuming a normal distribution.

SURVIVAL ANALYSIS RESULTS

Table 1 shows results of the survival analysis upon which the Markov transition probabilities were based. The regression shown here is for a drop of one Snellen visual acuity state. In the Markov model, transitioning from one state of visual health to the next worse state (that is, one Snellen drop) depends on one's baseline visual acuity and values of the other covariates in the model from the regression shown.

MARKOV MODEL RESULTS

Tables 2 and 3 show the results of the cost effectiveness analyses. Two sets of results are shown in each table, one for a cohort with a starting visual acuity of 20/40 and one starting at 20/100. This range represents both the best and average visual acuity from the trial. Table 2 shows cost effectiveness ratios from the government perspective, and table 3 shows results when only treatment costs are included.

From the government perspective, over the 2 year period, the expected incremental cost effectiveness ratios range from £286 000 (starting VA 20/100) to £76 000 (starting VA 20/40) per QALY gained and from £14 000 (20/100) to

Table 4 Sensitivity analysis

	Values	Government perspective	PDT cost only
Cost per QALY, 5 year time frame, cohort with best corrected visual acuity = 20/40 (in £000)			
Base case		9	38
Government perspective, low estimate	£1325/year	32	NA
Angiogram follow up*	£2640 (angiogram+outpatient visit every 3 months after PDT treatment ends)	24	54
Cost per QALY, 5 year time frame, cohort with best corrected visual acuity = 20/100 (in £000)			
	Values	**Government perspective**	**PDT cost only**
Base case		30	69
Government perspective, low estimate	£1325/year	61	NA
Angiogram follow up*	£2640 (angiogram+outpatient visit every 3 months after PDT treatment ends)	58	97

*In the base case, it is assumed that an angiogram is used for follow up only during the course of treatment. This sensitivity analysis assumes PDT treated patients have an angiogram and outpatient visit every 3 months for the entire period of the model for follow up, regardless of whether or not PDT is being given. This is in addition to standard follow up being done for non-PDT treated patients.

£34 000 (20/40) per vision year gained. A 5 year perspective yields incremental ratios less than £5000 for vision years gained and from £9000 (20/40) to £30 000 (20/100) for QALYs gained. Without societal or NHS cost offsets included, the 2 year incremental cost per vision year gained ranges from £20 000 (20/100) to £40 000 (20/40), and the 2 year incremental cost per QALY gained ranges from £412 000 (20/100) to £90 000 (20/40). The 5 year time frame shows expected costs of £7000 (20/40) to £10 000 (20/100) per vision year gained and from £38 000 (20/40) to £69 000 (20/100) per QALY gained.

Table 4 shows the results of several sensitivity analyses on two cohorts followed for 5 years, one with a starting visual acuity of 20/40 and one with a starting visual acuity of 20/100. Using the low estimate of the government perspective costs increases the cost effectiveness ratio by about threefold (from £9000 per QALY gained to £32 000 for the 20/40 cohort, and from £30 000 per QALY to £89 000 for the 20/100 cohort). Changing the assumption of follow up so that PDT treated patients receive an angiogram every 3 months (even after treatment with PDT ends), increases the cost per QALY gained by about £15 000 for those starting at 20/40 and about £30 000 for those starting at 20/100.

Figure 1 shows the cost effectiveness acceptability curve (CEAC) at 5 years for cohorts beginning treatment at 20/40 and at 20/100, from the government perspective and considering cost of treatment only. The CEACs shown here are a graphical display of the probability of a therapy being cost effective at a given level of willingness to pay for a QALY. For example, at a willingness to pay of £30 000 or less, PDT is cost effective for those starting treatment at 20/40 less than 30% of the time under the treatment cost only scenario, but almost 80% under the government perspective. At the same willingness to pay, PDT is cost effective for those starting treatment at 20/100 less than 5% of the time under the treatment cost only scenario, and about 45% of the time from the government perspective.

DISCUSSION

Our modelling suggests that, in terms of QALY gains, treating predominantly classic, subfoveal AMD lesions using PDT with verteporfin has a better chance to be cost effective when initiated at better levels of visual acuity. The estimated incremental gain in vision years from treatment is smaller when initiated at a higher level of baseline visual function. The differing results for the two outcomes reflect the non-linear nature of the estimated function of vision loss and illustrate how the two outcomes differentially weight the time spent in a given vision state. The anticipated treatment value for money becomes greater as follow up increases and more cost offsets are included in the analysis. An examination of tables 2 and 3 shows that over the short term (2 years), there is little difference in the results between a government perspective or considering treatment costs only, but the two perspectives show a much larger proportional difference at 5 years.

Since PDT therapy may be more cost effective in patients with better visual acuity (and therefore, at an earlier stage of disease), screening those at risk may be a practical method of deploying this technology. Additional work would be needed to quantify the efficiency of such an approach.

Anecdotal evidence suggests that clinicians are treating patients with fewer courses of therapy than in the TAP trial (that is, 2–3 versus 5–6). To the extent that this is the case, the cost effectiveness ratios produced by our model will be approximately halved, assuming that similar outcomes are observed. Further study should determine whether similar outcomes would accrue with fewer treatments.

These results are applicable only where the treated eye is the better seeing eye and has subfoveal, predominantly classic CNV. If the worse seeing eye (often the first eye involved with AMD) is treated, the results shown here are probably too optimistic. Further, if the treatment is used outside the context of those with predominantly classic, subfoveal CNV, these results would not apply.

The base case gains predicted by the model come largely from extending the time horizon beyond the trial period. The additional data from follow up of the trial's PDT arm suggests that there is clinical benefit beyond 2 years, so modelling this potential gain is relevant and useful.

The results here are sensitive to several of the assumptions. Incorporation of social care costs is clearly significant, as is the time frame over which benefits are modelled and the starting visual acuity. Additionally, the assumptions regarding follow up treatment are important, almost tripling the cost per QALY estimate for the treatment cost only perspective. These factors must be considered carefully in policy decisions about PDT's place in therapy.

A limitation of this work is that the primary outcome measure used, visual acuity as measured by the Snellen score, may not adequately capture the full known effects of PDT. For example, PDT has been shown to benefit contrast sensitivity,[5] and contrast sensitivity correlates well with visual function.[12] However, visual acuity also correlates very well with visual function[12 14] and has a clinical appeal as an overall measure of visual function and quality of life.

There are now open label follow up data for up to 4 years on 58% of the TAP trial treatment arm.[15] These data are not placebo controlled, and not all patients in the original study entered the extension phase; it only included patients for whom continued PDT might reduce further vision loss. These data may represent a biased sample of patients who would be treated with PDT, and should thus be interpreted with caution. These data show a loss of three lines of vision in 36% of patients at 24 months, 41% at 36 months, and 43% at 48 months. It may be that these data are indicative of either a stabilisation or increased slowing in vision loss—which would imply that our model is too conservative, because the model's treated arm experiences a continued decline in visual function. Alternatively, it may be the result of the natural disease process, implying that our model produces results biased towards PDT. Further follow up using an intention to treat design would be beneficial to clinicians and policy makers.

We based our model on a prospectively planned subgroup analysis from the TAP trial. Because it was a subgroup and not the entire population treated, these results only apply in a situation where those treated have predominantly classic disease—it should be clearly noted that patients without predominantly classic disease in the TAP population did not fare as well with verteporfin treatment. One additional criticism is the possibility that the clinical effects found in the subgroup are solely the result of chance. We chose this subgroup because it is the patient population and data upon which regulatory agencies have based the drug's licensure.

CONCLUSION

This analysis focuses on only those with a particular form of exudative AMD (predominantly classic, subfoveal CNV). Our evaluation suggests that early treatment (that is, treating eyes at less severe stages of disease) with PDT leads to increased efficiency. When considering only the cost of therapy, treating people at lower levels of visual acuity would probably not be considered cost effective. However, a broad perspective that incorporates other NHS treatment costs and social care costs suggests that over a long period of time, PDT may yield reasonable value for money. Consideration should

be given to early detection and treatment, particularly in the second eye to become involved. Further study aimed at potential screening may yield clues to an optimal use of PDT.

Authors' affiliations

D H Smith, Kaiser Permanente, Center for Health Research, Portland Oregon, USA, Centre for Health Economics, University of York, York, UK
P Fenn, Nottingham University Business School, Nottingham, UK
M Drummond, Centre for Health Economics, University of York, York, UK

Funding: This study was sponsored by Novartis AG, Switzerland. The contract gave full rights of publication to the investigators.

REFERENCES

1 **Evans J**, Wormald R. Is the incidence of registrable age related macular degeneration increasing? *Br J Ophthalmol* 1996;**80**:9–14.
2 **Klein R**, Klein K, Linton K. Prevalence of age-related maculopathy: the Beaver Dam Eye Study. *Ophthalmology* 1992;**99**:933–45.
3 **Fine SL**, Berger J, Maguire MG, *et al*. Drug therapy: age related macular degeneration. *N Engl J Med* 2000;**342**:483–92.
4 **Williams R**, Brody B, Thomas R, *et al*. The psychosocial impact of macular degeneration. *Arch Ophthalmol* 1998;**116**:514–20.
5 **Bressler NM**. Photodynamic therapy of subfoveal choroidal neovascularization in age-related macular degeneration with verteporfin: two-year results of 2 randomized clinical trials—TAP report 2. *Arch Ophthalmol* 2001;**119**:198–207.
6 **Brown G**, Sharma S, Brown M, *et al*. Utility values and age-related macular degeneration. *Arch Ophthalmol* 2000;**118**:47–51.
7 **Meads C**, Salas C, Roberts T, *et al*. Clinical effectiveness and cost utility of photodynamic therapy for wet age-related macular degeneration (www.nice.org.uk/Docref.asp?d=30223). Birmingham, West Midlands: Health Technology Assessment Group, University of Birmingham, 2002.
8 **Sharma S**, Brown GC, Brown MM, *et al*. The cost-effectiveness of photodynamic therapy for fellow eyes with subfoveal choroidal neovascularization secondary to age-related macular degeneration. *Ophthalmology* 2001;**108**:2051–9.
9 **HM Treasury Great Britain**. *Economic appraisal in central government: a technical guide for government departments*. London: HMSO, 1991.
10 **Smith D**, Drummond M, Fenn P. Modelling the long term benefits of photodynamic therapy (PDT) with vertoporfin for age related macular degeneration. CHE Discussion Paper Series 2002;DP187.
11 **Blumenkranz MS**, Bressler NM, Bressler SB, *et al*. Verteporfin therapy for subfoveal choroidal neovascularization in age-related macular degeneration: three-year results of an open-label extension of 2 randomized clinical trials—TAP Report no 5. *Arch Ophthalmol* 2002;**120**:1307–14.
12 **Riusala A**, Sarna S, Immonen I. Visual function index (VF-14) in exudative age-related macular degeneration of long duration. *Am J Ophthalmol* 2003;**135**:206–12.
13 **Miller J**, Schmidt-Erfurth U, Sickenberg M, *et al*. Verteporfin therapy of subfoveal choroidal neovasularization in age-related macular degeneration: results of two randomized clinical trials. *Arch Ophthalmol* 1999;**17**:1161–73.
14 **Mackenzie PJ**, Chang TS, Scott IU, *et al*. Assessment of vision-related function in patients with age-related macular degeneration. *Ophthalmology* 2002;**109**:720–9.
15 **National Institute for Clinical Excellence**. Final appraisal determination: photodynamic therapy for age-related macular degeneration (www.nice.org.uk/article.asp?a=32774). Accessed 6 December 2002.