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

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Record Status
This is a critical abstract of an economic evaluation that meets the criteria for inclusion on NHS EED. Each abstract contains a brief summary of the methods, the results and conclusions followed by a detailed critical assessment on the reliability of the study and the conclusions drawn.

Health technology
Photodynamic therapy (PDT) with verteporfin was assessed in patients with age-related macular degeneration (AMD). Dosage levels were not reported.

Type of intervention
Treatment.

Economic study type
Cost-utility analysis.

Study population
The study population comprised patients presenting with AMD subfoveal choroidal neovascularisation (CNV) lesions. Two hypothetical cohorts of men aged 75 years at the start of therapy were then used in a modelling element of the study. One cohort had a starting visual acuity (VA) of 20/40 and the other one of 20/100.

Setting
The setting was secondary care. The economic study was carried out in the UK.

Dates to which data relate
The effectiveness data related to a single published study (Bressler, see Other Publications of Related Interest). The costing data were taken from a NICE technology assessment report on PDT published in 2002 (Meads et al., see Other Publications of Related Interest) and were reported in December 2000 prices.

Source of effectiveness data
The effectiveness data were derived from a single study.

Link between effectiveness and cost data
The costing was carried out retrospectively on a different sample of patients to that used in the effectiveness study.

Study sample
The effectiveness data were taken from a study published in 2001 (Bressler, see Other Publications of Related Interest). The details reported here relate only to those provided in the current study. The sample comprised patients presenting with AMD subfoveal CNV lesions having a greatest linear dimension of less than or equal to 5,400 micrometre, with some evidence of classic CNV and best corrected VA between 20/40 and 20/200. The authors did not report specific details of how the sample was selected, or whether power calculations were carried out to estimate the impact of chance.
on the results. The trial included 609 patients. Of these, 402 received PDT with verteporfin and 207 received placebo. There were no reports of patients refusing to participate, or patients excluded for any reason.

**Study design**

The analysis was based on a randomised placebo-controlled trial, in which one eye from each patient was randomised. The patients were followed for 2 years at 3-monthly follow-up visits. It was unclear whether the study was carried out in a single centre or multiple centres. There was no reported loss to follow-up. There was no reported blinding of the outcome assessment.

**Analysis of effectiveness**

The analysis seems to have been conducted on an intention to treat basis, although this was not stated explicitly. The primary health outcome was moderate vision loss, which was defined as the loss of less than three lines of VA (15 letters). The authors did not report the comparability of the patient groups at analysis, although this information might have been reported in the primary source.

**Effectiveness results**

Of those patients treated with verteporfin, 53% lost less than three lines of vision compared with 38% of placebo-treated eyes, (p<0.001).

For patients treated with verteporfin, 82% did not experience severe vision loss (defined as more than six lines, or less than 30 letters) compared with 70% of placebo-treated eyes, (p<0.001).

In patients with minimally classic lesions, PDT and placebo groups had similar visual outcomes (48% for verteporfin patients versus 44% of the placebo patients). However, patients with predominantly classic lesions who were given PDT had lower vision loss (59% of those verteporfin versus 31% of those on placebo). The statistical analysis was not reported.

**Clinical conclusions**

Clinical conclusions were not explicitly drawn as the results were presented in a parent study. Since the UK recommendations indicate that only patients with predominantly classic CNV should be treated with verteporfin, the analysis focused on the sub-set of 243 patients with that particular form of disease.

**Modelling**

A Markov model was used to combine the effectiveness data with the costing data over 2- and 5-year time horizons. The model incorporated health states ranging from visual acuity of 20/40 to worse than 20/800, plus the dead state. A survival analysis using a Weibull function was used to estimate daily transition probabilities, controlling for baseline VA, gender and age.

**Methods used to derive estimates of effectiveness**

Authors’ assumptions were used to supplement the effectiveness evidence for the model.

**Estimates of effectiveness and key assumptions**

The authors made the following assumptions.

There were 1.52 re-treatments per person from year 2 to year 3 and none thereafter, and re-treatment was independent of baseline visual acuity.

Once follow-up was completed, there would be no further follow-up visits for those patients in the PDT treatment arm.
The better seeing eye would normally be treated.

Approximately 92% of the patients eligible for PDT with verteporfin would not have been eligible for treatment with laser photocoagulation.

There was no allowance for improvement in vision associated with verteporfin treatment, only slowed deterioration.

### Measure of benefits used in the economic analysis

The summary measures of health benefits were the number of vision-years gained and the quality-adjusted life-years (QALYs) gained. The number of vision-years gained was derived from the time spent with VA of 20/200 or better, and was estimated via a survival analysis. The QALYs were estimated through health state values taken from a time trade-off study of 80 patients with AMD, which was published in 2000 (Brown et al., see Other Publications of Related Interest). The effects of adverse events were incorporated through changes in quality of life, using values from an earlier cost-effectiveness analysis on PDT (Sharma et al., see Other Publications of Related Interest). The benefits were discounted at a rate of 2%.

### Direct costs

The costing was carried out from the perspectives of the National Health Service (NHS; treatment costs only) and the government (incorporating cost offsets). The estimate of treatment costs only included the cost of verteporfin and disposables, laser, angiography, outpatient appointment and adverse events. Other costs associated with the government perspective included possible cost offsets in medical and social care (such as blindness registration, low vision aids, rehabilitation services, housing and council tax benefit, depression treatment, hip replacement community care and residential care). The estimates were taken from NICE’s technology assessment report on PDT with verteporfin that was published in 2002. This report incorporated information from a range of sources. More specifically, published national sources (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. The costs were discounted at a rate of 6%. All the costs were inflated to December 2000 prices. The analysis separated the categories of cost, but the unit costs were not reported separately from the quantities.

### Statistical analysis of costs

The costs were treated deterministically.

### Indirect Costs

The indirect costs were not estimated, which was appropriate given the perspective adopted.

### Currency

UK pounds sterling (€).

### Sensitivity analysis

One-way sensitivity analyses were carried out using the lower limit of the range of cost offsets and the low estimate for angiography follow-up. Cost-effectiveness acceptability curves were generated, varying transition probabilities and health state utilities, to assess the probability of verteporfin being cost-effective for different values of willingness-to-pay for health outcomes.

### Estimated benefits used in the economic analysis

The results presented are those from the broader perspective of the government.

Over a timeframe of 2 years with baseline VA of 20/40, the number of vision-years was 1.618 with placebo and 1.773
with verteporfin (difference 0.155). The number of QALYs was 1.136 with placebo and 1.205 with verteporfin (difference 0.069).

Over a timeframe of 2 years with baseline VA of 20/100, the number of vision-years was 1.074 with placebo and 1.383 with verteporfin (difference 0.309). The number of QALYs was 0.980 with placebo and 0.995 with verteporfin (difference 0.015).

Over a timeframe of 5 years with baseline VA of 20/40, the number of vision-years was 2.160 with placebo and 3.050 with verteporfin (difference 0.890). The number of QALYs was 2.205 with placebo and 2.375 with verteporfin (difference 0.170).

Over a timeframe of 5 years with baseline VA of 20/100, the number of vision-years was 1.222 with placebo and 1.858 with verteporfin (difference 0.636). The number of QALYs was 1.999 with placebo and 2.093 with verteporfin (difference 0.094).

**Cost results**
The results presented are those from the broader perspective of the government.

Over a timeframe of 2 years with baseline VA of 20/40, the cost of treatment was 1,275 with placebo and 6,490 with verteporfin (difference 5,215).

Over a timeframe of 2 years with baseline VA of 20/100, the cost of treatment was 4,590 with placebo and 8,878 with verteporfin (difference 4,288).

Over a timeframe of 5 years with baseline VA of 20/40, the cost of treatment was 10,200 with placebo and 11,700 with verteporfin (difference 1,500).

Over a timeframe of 5 years with baseline VA of 20/100, the cost of treatment was 15,700 with placebo and 18,500 with verteporfin (difference 2,800).

**Synthesis of costs and benefits**
The results presented are those from the broader perspective of the government.

Over a 2-year horizon with VA of 20/40, the cost per vision-year gained was 33,645 with verteporfin and the cost per QALY gained was 75,580.

Over a 2-year horizon with VA of 20/100, the cost per vision-year gained was 13,877 with verteporfin and the cost per QALY gained was 285,867.

Over a 5-year horizon with VA of 20/40, the cost per vision-year gained was 1,685 with verteporfin and the cost per QALY gained was 8,823.

Over a 5-year horizon with VA of 20/100, the cost per vision-year gained was 4,402 with verteporfin and the cost per QALY gained was 29,787.

The authors reported that the results were sensitive to several assumptions. In particular, the incorporation of social care costs, the timeframe over which the benefits were modelled, starting VA, and assumptions about follow-up treatment.

**Authors' conclusions**
Early treatment (i.e. treating eyes at less severe stages of disease) with photodynamic therapy (PDT) leads to increased efficiency. Over a long period of time, PDT may yield reasonable value for money. When considering only the cost of therapy, treating people at lower levels of visual acuity (VA) would probably not be considered cost-effective.
CRD COMMENTARY - Selection of comparators
The authors assessed PDT with verteporfin in comparison with treatment with placebo. PDT with verteporfin was reported to be a relatively recently available technology that had fewer side effects than available alternatives. Comparing this with placebo demonstrates the active value of the technology of interest.

Validity of estimate of measure of effectiveness
The effectiveness data were taken from a published study that was described in more detail elsewhere (Bressler, see Other Publications of Related Interest). The analysis was based on a randomised placebo-controlled trial. This design helps to minimise systematic differences between patient groups and so increases the internal validity of the study. The study sample comprised patients presenting with AMD and so was representative of the study population. The authors did not report power calculations, or the comparability of the patient groups at analysis. However, this information might have been reported in the parent study. The extent to which the primary study controlled for potential biases was not reported.

Validity of estimate of measure of benefit
The estimation of benefits was modelled. The Markov model used for this purpose was appropriate, as it enabled the estimation of long-term benefits obtained by adopting each of the strategies examined. All future benefits were discounted at a rate of 2% per annum in line with recommendations from the UK Treasury. The authors used vision-years gained and QALYs gained as their summary measures of benefit. These measures were a logical choice, offering results comparable to related studies as well as broader studies. However, the authors acknowledged that vision-years gained may not adequately capture the effects of PDT.

Validity of estimate of costs
The costing was carried out from two perspectives, the NHS and the government. The authors gave a breakdown of the components of each perspective, although they did not report the unit costs and the quantities separately. Although in principle this prevents the reader replicating the results in their own setting, the authors clearly stated that the cost estimates were taken from NICE's technology assessment report, thus further details may be obtained directly from this source. Any omissions or alterations in cost arising from alternative perspectives or settings may not influence the authors' principal conclusions, owing to the relatively large absolute differences in costs reported. Discounting was appropriately undertaken since the costs were incurred during a period of 2 to 5 years. The date to which the prices referred was reported, which improves the generalisability of the results.

Other issues
The authors did not compare their findings with other published results. This might have been due to PDT being a relatively new therapy and few, if any, results being available. The issue of generalisability was addressed both explicitly and implicitly. The authors discussed the implications for the results if new anecdotal evidence is true, and also highlighted that the results only apply to settings in which the treated eye is the better-seeing eye and where those treated have predominantly classic disease. The results do not appear to have been presented selectively as a range of results were given. Some of the results would appear to be conflicting, and the authors provided a valuable discussion to help explain this anomaly. The authors' conclusions accurately reflected both the scope of the study and the results presented. A number of limitations were presented. For example, VA may not necessarily capture the full effects of PDT, and further available data may not be based on intention to treat.

Implications of the study
The authors did not make any recommendations for policy or practice as a result of their study, although several suggestions for further work were made. Such suggestions included studies aimed at assessing the benefits of screening, early detection and treatment, and further follow-up using an intention to treat design.

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