The cost-effectiveness of photodynamic therapy for fellow eyes with subfoveal choroidal neovascularization secondary to age-related macular degeneration


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
The health intervention examined in the study was photodynamic therapy (PDT) for the treatment of subfoveal choroidal neovascularisation (CNV) secondary to age-related macular degeneration (AMD).

Type of intervention
Treatment.

Economic study type
Cost-utility analysis.

Study population
The study population comprised patients who had disciform degeneration in one eye and whose fellow better-seeing eye had predominantly classic CNV. The mean age of patients involved in the study was 75 years. Two distinct typical patients were considered: the first patient had 20/40 vision in the eye eligible for treatment (base case 1) and the second patient had a 20/200 vision in the treatment eye (base case 2).

Setting
The setting was not stated. The economic study was carried out in the USA.

Dates to which data relate
Data on effectiveness and resource use were derived from studies published between 1994 and 2000. The price year was 2000.

Source of effectiveness data
The effectiveness evidence was based on published studies and experts' assumptions.

Modelling
A decision tree model was constructed to assess costs and benefits of PDT in comparison with placebo. Two models were used in the analysis to assess the cost-utility of the interventions and were based on two different time horizons:

- a 2-year model was first selected as this was the observation period in one of the studies used to derive clinical data;
- an 11-year model was then used as this was the expected survival of the average patients in the study, as estimated from expected mortality rates.

As both models were applied to base cases 1 and 2, a total of four distinct analyses were conducted. The decision
models were based on two main Markov states: development or non-development of a three line vision loss, which represented an 'absorbing state' from which it is not possible to move to another health state.

**Outcomes assessed in the review**
The outcomes assessed from published studies and used as model inputs were expected mortality rates, measures of treatment efficacy, estimation of complications (visual disturbance, vitreous haemorrhage, retinal capillary nonperfusion, injection-site adverse events, infusion-related back pain, allergic reactions, and photosensitivity reactions) and utility values associated with such complications, and utility values of the health states included in the decision model.

**Study designs and other criteria for inclusion in the review**
The primary study used to derive data on patient population and treatment efficacy was based on two multicentre, double-masked, placebo-controlled, randomised clinical trials carried out in Europe and North America. Another study was a census survey. Details on the third study were not reported, but the authors stated that utility values were derived using the time-trade-off method on a sample of 80 patients.

**Sources searched to identify primary studies**
Not stated.

**Criteria used to ensure the validity of primary studies**
Not stated.

**Methods used to judge relevance and validity, and for extracting data**
Not stated.

**Number of primary studies included**
Three primary studies were used to derive the effectiveness evidence.

**Methods of combining primary studies**
Primary studies were combined using narrative methods.

**Investigation of differences between primary studies**
Not stated.

**Results of the review**
The results of the review were as follows:

The mean life expectancy of the typical patients considered in the study was 11 years.

Treatment efficacy was estimated using the proportion of patients receiving PDT or placebo who had a loss of 15 or more letters develop at 24 months: 0.313 (95% CI: 0.244 - 0.392) with PDT and 0.591 (95% CI: 0.482 - 0.701) with placebo.

The utility values were 0.57 (95% CI: 0.47 - 0.67) when patients developed 3-line visual loss and 0.81 (95% CI: 0.73 - 0.89) when patients did not develop 3-line visual loss in patients of case-base 1; and 0.40 (95% CI: 0.29 - 0.50) when patients developed 3-line visual loss and 0.52 (95% CI: 0.38 - 0.66) when patients did not develop 3-line visual loss in
patients of case-base 2.

The values of complication incidence for PDT and placebo were 17.7% and 11.6% for visual disturbance, 1% and 0.5% for vitreous haemorrhage, 0.2% and 1% for retinal capillary nonperfusion, 13.4% and 3.4% for injection-side adverse events, 2.2% and 0 for infusion-related back pain, 1.2% and 3.4% for allergic reactions, and 3% and 0 for photosensitivity reactions.

The utility values associated with complications were 1 for visual disturbance, 0.8 for vitreous haemorrhage, 0.95 for retinal capillary nonperfusion, 0.99 for injection-site adverse events and infusion-related back pain, 0.95 for allergic reactions, and 0.98 for photosensitivity reactions.

Methods used to derive estimates of effectiveness
Some of the effectiveness data were derived through a Delphi panel of four ophthalmologists.

Estimates of effectiveness and key assumptions
For the 11-year model, it was assumed that the treatment had an absolute risk reduction of 27.8% after 2 years and would decrease by 10% per year for the remaining 9 years. The proportion of patients who lose three or more lines of vision in the placebo group would stay constant at 59.1%.

Measure of benefits used in the economic analysis
The benefit measure used in the economic analysis was quality-adjusted life-year (QALY). Data on utility weights were estimated through the time-trade-off approach. A 3% discount rate was applied in the 11-year decision model.

Direct costs
A 3% discount rate was used as the time horizon of the model was 11 years. Unit costs and quantities of resources were not reported separately. Only incremental costs were included in the analysis, meaning that costs such as administration, labour hours, and capital expenditures, were assumed to be common to both interventions. The health service costs included in the economic evaluation were visit, fluorescin, angiography photographs, visudyne cost, and laser fee. The cost/resource boundary adopted in the study was that of the third-party payer. The estimation of costs was based on actual Medicare reimbursement rates, while resource use was estimated alongside the clinical trial used as source of efficacy data. It was assumed that 5.5 treatments were required in the two typical patients. The price year was 2000.

Statistical analysis of costs
Costs were treated deterministically.

Indirect Costs
Indirect costs were not included in the analysis.

Currency
US dollars ($).

Sensitivity analysis
Several one- and two-way sensitivity analyses were conducted to investigate the uncertainty regarding utility values and efficacy data used in the decision models. The ranges used in the analysis were the 95% confidence intervals reported earlier. A Monte Carlo simulation was also performed.
Estimated benefits used in the economic analysis
For the 2-year model, the expected utility values were 1.3243 with PDT and 1.1959 with placebo (increment of 10.73%) for base case 1; and 5.655 with PDT and 5.3993 with placebo for base case 2.

For the 11-year model, the expected utility values were 5.655 with PDT and 5.3993 with placebo for base case 1 and 3.8910 with PDT; and 3.7633 with placebo for base case 2.

Cost results
The incremental cost of PDT over placebo was $1,822 for one treatment, $3,909 for 2 treatments, $5,996 for 3 treatments, $8,083 for 4 treatments, $10,179 for 5 treatments, $12,257 for 6 treatments, $14,344 for 7 treatments, and $16,431 for 8 treatments. Total costs as estimated in the two decision models were not reported.

Synthesis of costs and benefits
An incremental cost-utility analysis was performed to combine costs and QALYs of PDT over placebo.

For the 2-year model, the extra cost per QALY with PDT was $86,721 for base case 1 and $173,984 for base case 2.

For the 11-year model, the extra cost per QALY with PDT was $43,547 for base case 1 and $87,197 for base case 2.

The estimated cost per QALY was affected by the number of treatments required and by the use of utility values reported in the upper end of the confidence intervals. In addition, in patients with poor presenting vision, the cost per QALY of PDT could be greater than $1,000,000. The model was quite robust to variations in other inputs.

Authors’ conclusions
The authors concluded that PDT proved to be a cost-effective treatment only in patients with a good visual acuity at baseline, but from the perspective of the third-party payer it was not convenient for the treatment of those patients with poor visual acuities.

CRD COMMENTARY - Selection of comparators
The rationale for the choice of the comparator was clear. Placebo was selected as the main aim of the study was to assess the active value of PDT. You, as a user of this database, should decide whether no treatment represents a valid comparator in your own setting.

Validity of estimate of measure of effectiveness
The analysis of effectiveness was mainly based on a published study, which was used to derive data on patient population and efficacy of the intervention. These data were then combined with other published data using narrative methods. As a result, a formal review of the literature was not undertaken. Data on utility values used to calculate QALYs and complications were based on authors’ experience and a group of four ophthalmologists forming a Delphi panel. These estimates were investigated in the sensitivity analyses.

Validity of estimate of measure of benefit
QALYs were used as benefit measures in the economic analysis. Utility weights were derived from the authors’ previous research based on the time-trade-off approach. The use of QALYs enhanced the comparability of the outcome of PDT with the benefits of other interventions implemented in the health care system.

Validity of estimate of costs
The analysis of costs was conducted from the perspective of the third-party payer and it appears that all relevant categories of costs were included in the analysis. The price year was reported, thus making deflation exercises in other
settings easier. Appropriate discounting was applied. The sources of data regarding costs and resource use were reported. However, unit costs were not reported separately from quantities of resources. Costs were treated deterministically in the base case and no sensitivity analyses were performed.

Other issues
The authors compared PDT with other therapies, although they commented that comparisons may be difficult due to the fact that data used are often of different quality. The issue of the generalisability of the study findings to other settings was not addressed, but several sensitivity analyses were conducted, thus enhancing the external validity of the analysis. The study referred to a sample of patients with CNV secondary to AMD and this was reflected in the conclusions of the analysis. The authors discussed the potential limitations of using physician-derived utility values instead of patient-derived utilities, but this choice was justified by the lack of reliable data in the literature. The authors also acknowledged that some of the assumptions made in the 11-year decision model may have been unreliable, but sensitivity analyses were conducted to investigate such assumptions.

Implications of the study
The authors noted that PDT led to improvements in patients' quality of life, but at current prices its cost-effectiveness was not clear from the perspective of a for-profit third-party payer. The use of long-term data from clinical trials could provide new reliable information for carrying out an economic evaluation with a longer time horizon.

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