A value-based medicine comparison of interventions for subfoveal neovascular 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 study examined three treatments for elderly patients with subfoveal neovascular macular degeneration. These were laser photocoagulation, intravitreal pegaptanib therapy, and photodynamic therapy using verteporfin (PDT). All three strategies were compared with a reference case of no intervention.

Type of intervention
Treatment.

Economic study type
Cost-utility analysis.

Study population
The study population comprised a hypothetical cohort of patients with classic, subfoveal choroidal neovascularisation associated with age-related macular degeneration. Patients with minimally classic and occult lesions were not considered. An average age of 75 years was considered for the analysis.

Setting
The setting was secondary care and a hospital. The economic study was carried out in the USA.

Dates to which data relate
The clinical data came from studies published between 1991 and 2005. The resource use data were derived from studies published between 1991 and 2006. The price year was 2005.

Source of effectiveness data
The clinical data used in the analysis were the clinical effectiveness of the three treatments (defined in terms of visual acuity), the side-effects of therapy, and survival of a typical 75-year-old patient.

Sources searched to identify primary studies
Clinical data on treatment effectiveness and side-effects came from published clinical trials (the Macular Photocoagulation Study, the Pegaptanib for Neovascular Age-Related Macular Degeneration Study, the Treatment of Age-Related Macular Degeneration with Photodynamic Therapy Study), the main characteristics and results of which were described. Survival was estimated using life tables.

Methods used to judge relevance and validity, and for extracting data
The primary studies appear to have been identified selectively. No systematic search for data was reported. However,
the data were derived from randomised clinical trials, which should ensure a high internal validity.

**Measure of benefits used in the economic analysis**
The summary benefit measure used was the expected number of quality-adjusted life-years (QALYs). These were estimated by combining average survival (which was the same for the three treatments) with data on QoL. QoL was estimated from a cohort of 233 patients with age-related macular degeneration using the time trade-off approach. These data were then matched to the improvement in visual acuity derived from the clinical trials. Utility decrements associated with the side-effects of therapy were also used to calculate overall QoL. The QALYs were discounted at an annual rate of 3%.

**Direct costs**
The analysis of costs was performed from the viewpoint of the third-party payer. It included the costs associated with initial consultation, office visits, fluorescein angiography, verteporfin, pegaptanib, laser photocoagulation, intraocular injection and physician time for PDT. Some unit costs were presented separately from the quantities of resources used. The costs were derived from several sources, including Medicare reimbursements for hospitals, pharmaceuticals and other providers, using Current Procedural Terminology codes. Resource consumption was mainly derived from published sources. Discounting was relevant, given that the long-term costs were considered, and an annual rate of 3% was applied. The price year was 2005.

**Statistical analysis of costs**
The costs were treated deterministically.

**Indirect Costs**
Productivity costs were not considered.

**Currency**
US dollars ($).

**Sensitivity analysis**
A deterministic sensitivity analysis was carried out to assess the robustness of the cost-utility ratios to variations in utility values (+/- 10%), effectiveness of treatment (+/- 20%), costs (+/- 20%) and discount rate (0% and 5%). The range of values was selected arbitrarily.

**Estimated benefits used in the economic analysis**
Over 12 years, the expected improvements in discounted (undiscounted) QALYs with respect to no treatment were 0.246 (0.301) with laser photocoagulation, 0.363 (0.438) with pegaptanib and 0.491 (0.585) with PDT. The improvement in QALYs was significantly higher with pegaptanib over laser photocoagulation and with PDT over pegaptanib.

**Cost results**
Over 12 years, the total discounted (undiscounted) costs were $15,488 ($16,348) with PDT, $24,314 ($25,589) with pegaptanib and $2,012 ($2,012) with laser photocoagulation.

**Synthesis of costs and benefits**
Average cost-utility ratios were calculated in order to combine the costs and benefits of the alternative strategies.
The average cost per QALY gained with respect to no intervention was $8,179 (undiscounted $6,684) with laser photocoagulation, $66,978 (undiscounted $59,787) with pegaptanib therapy and $31,544 (undiscounted $27,945) with PDT.

Incremental cost-effectiveness ratios were not calculated, but the costs and benefits showed that pegaptanib therapy was dominated by PDT.

The results of the sensitivity analysis did not substantially alter the base-case findings. Overall, all the cost-utility ratios fell within the threshold of $100,000 per QALY, which suggests that the interventions are cost-effective.

Authors’ conclusions
Photodynamic therapy (PDT) was the most cost-effective treatment for patients with classic, subfoveal choroidal neovascularisation, given its high patient value.

CRD COMMENTARY - Selection of comparators
The rationale for the choice of the comparators was clear in that three widely used treatments for patients with subfoveal neovascular macular degeneration were considered. You should decide whether they are valid comparators in your own setting.

Validity of estimate of measure of effectiveness
The clinical data might have been identified selectively as a systematic review of the literature was not described. The selection of clinical trials as the source of treatment effectiveness was appropriate since these trials are usually associated with a high internal validity. Details of follow-up and randomisation for each trial were described.

Validity of estimate of measure of benefit
The use of QALYs as the summary benefit measure was appropriate given the objective of the analysis and the impact of the disease on QoL. Extensive information on the source of QoL data was provided. Discounting was performed and the impact of no discounting or other discount rates was investigated in the sensitivity analysis.

Validity of estimate of costs
The cost categories included were consistent with the viewpoint of the analysis. Some information on the unit costs and quantities of resources used was given, which will enable the analysis to be replicated in other settings. The sources of the costs were stated and were consistent with the perspective of the study. Typical US sources were chosen. Statistical analyses of the cost estimates were not performed, but the total costs were varied slightly in the sensitivity analysis. The price year was reported, which will facilitate reflation exercises in other time periods.

Other issues
The authors did not make extensive comparisons of their findings with those from other studies. They also did not explicitly address the issue of the generalisability of the study results to other settings. Few sensitivity analyses were conducted and the external validity of the study would appear low. The authors highlighted some potential limitations of the analysis. First, the analysis did not include lesions larger than 6 disc areas. Second, clinical trials for pegaptanib and PDT did not provide data beyond 2 years. Third, the current analysis was a second eye analysis. The use of an incremental analysis to compare the three treatments directly would have been more appropriate than an average cost-utility analysis. Both discounted and undiscounted results were given. The results of the analysis were presented satisfactorily.

Implications of the study
The study results support the use of PDT for the treatment of classic, subfoveal neovascular macular degeneration. The
authors suggest that a further analysis should be performed as soon as data on ranibizumab become available.

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**Indexing Status**
Subject indexing assigned by NLM

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