Cost-effectiveness of adjunctive hyperbaric oxygen in the treatment of diabetic ulcers
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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
The adjunctive use of hyperbaric oxygen (HBO2) therapy in the treatment of diabetic ulcers.

Type of intervention
Treatment.

Economic study type
Cost-utility analysis.

Study population
The study population comprised a hypothetical cohort of 1,000 patients with severe diabetic foot ulcers (Wagner's classification III or above). The patients were assumed to be 60 years old. The exclusion criteria (in fact, assumptions) were no contraindications to HBO2 therapy, and no high fever, emphysema or pneumothorax.

Setting
The setting was not reported. The economic analysis was conducted in the USA.

Dates to which data relate
The effectiveness data were obtained from studies published between 1965 and 2000. The resource data were gathered from a study published in 1995 and Hyperbaric Oxygen Therapy Association data published in 2002. The price year was 2001.

Source of effectiveness data
The effectiveness data were derived from a review of the literature.

Modelling
A decision analytic model was constructed to estimate the cost-effectiveness of adjunctive use of HBO2 therapy. Four treatment outcomes were defined. These were primary healed, minor lower extremity amputation (LEA), major LEA and death. Three time intervals (1, 5 and 13 years) were chosen for the outcome assessment. The 5-year interval was chosen to represent the private payers' perspective, while the 12-year interval was selected to represent the societal perspective. Justification for these choices was provided.

Outcomes assessed in the review
The outcomes assessed in the review were the rate of healing, the rate of LEAs, the mortality rates and the EuroQol weights (EQ-5D) to treatment outcomes.
Study designs and other criteria for inclusion in the review
The probabilities of treatment outcomes (healing and LEA rates) were derived from the summarised results of four clinical studies. The inclusion criteria for the review were prospective controlled design, diabetic etiology, and the measure of treatment outcomes as primary healing and healing with minor and major LEAs. The mortality rate and the EuroQol weights were derived from different published studies.

Sources searched to identify primary studies
The four prospective, controlled studies were selected through a complete MEDLINE search between 1985 and 2001. Five studies were excluded because they failed to meet one of the inclusion criteria.

Criteria used to ensure the validity of primary studies
The criteria used were not reported. However, the authors reported the small size of each study sample from the included studies (35 versus 33 patients, 15 versus 15, 18 versus 5 and 4 versus 1).

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

Number of primary studies included
Four prospective, controlled studies were included in the analysis of treatment outcomes. One study was included in the analysis of EuroQol weights. One study was included in the analysis of mortality rates.

Methods of combining primary studies
Not reported.

Investigation of differences between primary studies
Not reported.

Results of the review
The rate of healing with HBO2 was 55% (worst case 31%; best case 89%).

The rate of healing without HBO2 was 33% (worst case 30%; best case 20%).

The rate of major LEAs with HBO2 was 10% (worst case 9%; best case 11%).

The rate of major LEAs without HBO2 was 41% (worst case 33%; best case 80%).

The rate of minor LEAs with HBO2 was 35% (worst case 60%; best case 0%).

The rate of minor LEAs without HBO2 was 26% (worst case 37%; best case 0%).

The mortality rate of primarily healed was 2.8%.

The mortality rate of minor LEAs was 2.8%.

The mortality rate of major LEAs was 16.3%.

The EQ-5D weight of primarily healed was 0.6.

The EQ-5D weight of minor LEAs was 0.6.
The EQ-5D weight of major LEAs was 0.31.

The EQ-5D weight of death was 0.

**Methods used to derive estimates of effectiveness**
The authors made two assumptions for the analysis.

**Estimates of effectiveness and key assumptions**
The mortality rate was assumed to be constant over the 12-year period. Foot ulcers were assumed not to recur once they were healed.

**Measure of benefits used in the economic analysis**
The benefit measures were the number of minor and major LEAs averted, and the number of discounted quality-adjusted life-years (QALYs) gained. The QALYs were derived from assigning EuroQol weights that were derived from a published study (see utility values in the ‘Results of the Review’ section). The benefits were discounted at a rate of 3%.

**Direct costs**
Two perspectives were adopted, the payer and society. However, only the direct costs were included in the analysis. The direct costs estimated were for HBO2 treatment and the averted treatment costs of minor and major LEAs. The costs of HBO2 treatment included technical and physician fees. The averted treatment costs covered surgery, inpatient care, rehabilitation, first-year outpatient visits, and physician fees. The cost of wound care treatment was excluded from the analysis because it was similar for both treatment groups. The authors also excluded the costs of treating side effects of HBO2 therapy because major side effects requiring medical attention rarely occur. The resource quantities and unit costs were derived from the literature. All the costs were inflated to 2001 dollars. The resource quantities and the costs were not reported separately. It appears that the costs have not been discounted, whereas the benefits were.

**Statistical analysis of costs**
No statistical analysis on the costs was performed.

**Indirect Costs**
The indirect costs were not included.

**Currency**
US dollars ($).

**Sensitivity analysis**
Sensitivity analyses were conducted to measure the range of the cost-effectiveness ratios between the least and most efficacious outcomes of HBO2 therapy. One-way sensitivity analyses were undertaken to evaluate the impact of each parameter on the cost-effectiveness ratios of the base-case estimation in different time periods.

**Estimated benefits used in the economic analysis**
A total of 165 major LEAs were averted with the adjunctive use of HBO2 therapy (205 LEAs in the control group versus 50 LEAs in the HBO2 group).

There was an increase of 45 cases of minor LEAs in the HBO2 group (130 LEAs in the control group versus 175 LEAs
in the HBO2 group).

Approximately 50.2 (year 1), 265.3 (year 5) and 608.7 QALYs (year 12) were gained due to the use of HBO2 therapy.

**Cost results**
The total cost was $5,901,500 for HBO2 therapy (A), $1,773,780 for additional minor LEAs (B), and $6,304,305 for major LEAs averted (C).

The incremental cost of the adjunctive use of HBO2 therapy was $1,370,965 (A+B-C) compared with conventional wound care.

**Synthesis of costs and benefits**
Compared with conventional wound care, the incremental cost per additional QALY gained of the adjunctive use of HBO2 therapy was $27,310 (1-year), $5,166 (5-year) and $2,255 (12-year) for the three time periods considered.

The results were very sensitive to the probabilities of the treatment outcomes.

The cost-effective ratios were most sensitive to the quality weights, especially for major LEA.

The number of HBO2 treatments per case, the HBO2 cost per treatment, and the treatment costs of major and minor LEA per case, also had a significant impact on the cost-effectiveness ratios.

The cost-effectiveness ratios were less sensitive to the mortality rate and discount rate.

**Authors' conclusions**
Hyperbaric oxygen (HBO2) therapy in the treatment of diabetic ulcers is cost-effective, particularly from a long-term perspective.

**CRD COMMENTARY - Selection of comparators**
The reason for the choice of the comparator (conventional care) was clear. You should decide if this represents a valid comparator in your own setting.

**Validity of estimate of measure of effectiveness**
The authors reported that a systematic review of the literature was conducted. Prospective, controlled trials were used as primary studies in the analysis of probabilities of treatment outcomes. The authors used estimates from a published study to estimate EuroQol weights. The validity of those studies was not reported in the methodology section. However, the authors reported in their discussion that the cost-effectiveness estimation was based on a limited number of small and methodologically weak studies. No sensitivity analyses were performed on these estimates. Consequently, the validity of the study was strongly limited by the clinical studies that were the basis of the analysis. The assumption of no recurrence of foot ulcers may have biased the results in favour of HBO2 therapy.

**Validity of estimate of measure of benefit**
The estimation of benefits was modelled. The decision analysis model used to derive the measure of health benefit appears to have been appropriate. Utility weights were derived from another study. The validity of the method used to derive the EuroQol weights was not reported. However, a sensitivity analysis was carried out on those estimates.

**Validity of estimate of costs**
The authors reported that they adopted a societal perspective, although they did not include the indirect costs. The exclusion of these costs might have biased the results in favour of the HBO2 therapy (important psychological costs...
relative to combination therapy). Other costs were excluded from the analysis. For example, the cost of wound care treatment because it was similar for both treatment groups, and the costs of treating side effects of HBO2 therapy. Thus, the costs of HBO2 therapy were underestimated. The resource quantities and the costs were not reported separately. Health resource use was not derived from actual data but from published sources. These facts do not allow the analysis to be reworked for other settings. A sensitivity analysis was performed on the costs, but the ranges of variation and results were not reported in detail. Discounting was not performed on the costs, although the cost were incurred during a 12-year interval.

**Other issues**
The authors provided little discussion of the generalisability of their results. They did not compare their findings with those from other studies. The authors highlighted some limitations of their study. The results do not appear to have been reported selectively.

**Implications of the study**
The authors concluded that more clinical trials of HBO2 therapy with randomised controlled designs, larger sample sizes, and especially, long-term follow-up of patients, are needed to improve the estimation.

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None stated.

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