Cost-effectiveness of treating deep diabetic foot ulcers with Promogran in four European countries

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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 use of Promogran, a dressing containing 55% collagen and 45% oxidised regenerated cellulose, in conjunction with good wound care (GWC) for the treatment of non-superficial diabetic foot ulcers. GWC was defined as sharp debridement, wound cleansing and the application of a dressing.

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
The authors used a hypothetical cohort of patients. The only detail reported was that initially all patients had an uninfected diabetic foot ulcer. However, the transition probabilities were mainly derived from a study population with neuropathic diabetic foot ulcers. Correspondence with the authors has confirmed that the patient population comprised those patients with neuropathic diabetic foot ulcers.

Setting
The setting was secondary care. The study models the results of treatment in France, Germany, Switzerland and the UK.

Dates to which data relate
The effectiveness data were taken from papers published between 1994 and 2000 and one paper that was in press (at the time of publication of this article). The date to which the resource use data related was not reported. All prices were converted to 2000 values.

Source of effectiveness data
The effectiveness data were derived from a non-systematic review or synthesis of completed studies, augmented by expert opinion.

Modelling
A Markov state transition model was used to estimate the probability of wounds healing, becoming infected, gangrene developing, an ulcer healing after amputation, and death. The model was run for one year with a cycle length of one month. It was not possible for a patient to progress from having an uninfected ulcer to gangrene or amputation. The model did not allow gangrene to be healed without amputation. Infected ulcers could heal without amputation, but only after two transitions.
Outcomes assessed in the review
The authors did not report any details of the effectiveness or epidemiological data obtained from the review. The transition probabilities derived from this data were reported, but no further details were given.

Study designs and other criteria for inclusion in the review
The paper did not report any inclusion or exclusion criteria that the authors used to identify primary sources of evidence. The efficacy of Promogran on uninfected neuropathic ulcers was taken form an RCT. The transition probabilities were derived from prospective studies. No further details are reported.

Sources searched to identify primary studies
Not reported.

Criteria used to ensure the validity of primary studies
Not reported.

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

Number of primary studies included
The study drew evidence from at least five papers to establish the effectiveness of the intervention and transition probabilities.

Methods of combining primary studies
The efficacy of Promogran was taken from a single study. The estimate of the probability of amputation with gangrene and the subsequent health states appear to have been taken from three studies. The other transition probabilities were derived form a number of studies. However, the methods used to combine the results were not reported.

Investigation of differences between primary studies
Not reported.

Results of the review
The transition probabilities were reported in the paper. No other results were reported.

Methods used to derive estimates of effectiveness
Expert opinion was used to supplement the data obtained from the review.

Estimates of effectiveness and key assumptions
The experts estimated that 80 to 85% of ulcer-related amputations were due to infection. In addition, they assumed the Promogran dressing would be changed every 48 hours, or 16 times a month.

Measure of benefits used in the economic analysis
The authors did not derive a summary measure of benefit. A cost-consequences analysis was therefore undertaken. The intermediate model outcomes were the number of ulcers healed and the number of amputations prevented.
Direct costs
The study reported the costs incurred by the health care provider. The cost of Promogran dressings in each of the four countries was obtained directly from Johnson and Johnson affiliates in each country. The authors assumed the number of dressings required. The quantity of other resources used by the two treatments was obtained through interviews with physicians. The source of the cost information was not reported. The costs were split into broad categories (i.e. antibiotics, inpatient care), but the authors did not provide a complete breakdown of the resource quantities and unit costs. The costs were only calculated for the period of the model (one year). The costs were not discounted, which was appropriate given the time scale of the study. However, a 5% rate was used in the sensitivity analysis. All the costs were reported for the year 2000.

Statistical analysis of costs
The cost data were treated deterministically.

Indirect Costs
No indirect costs were included in the analysis.

Currency
Euros (Euro).

Sensitivity analysis
Sensitivity analyses were carried out to consider variability in the data. The effectiveness of Promogran and GWC in healing ulcers was varied. In addition, the frequency of changing the Promogran dressing, the maximum treatment time with Promogran, and disallowing treatment with Promogran for recurring ulcers, were also investigated. The analysis was one-way.

Estimated benefits used in the economic analysis
Twelve-month treatment with Promogran and GWC resulted in 56.1 healed ulcers per 100 patients, compared with 60.3 per 100 patients amongst those who received GWC alone. The number of amputations was also lower in the Promogran group (6.26 per 100 patients) than the GWC alone group (6.50 per 100 patients).

Cost results
The total cost of treatment with Promogran and GWC over 12 months was Euro 11,485 in France, Euro 8,172 in Germany, Euro 14,040 in Switzerland and Euro 16,191 in the UK.

GWC alone cost Euro 11,654 in France, Euro 8,455 in Germany, Euro 14,290 in Switzerland and Euro 17,270 in the UK.

No confidence intervals or statistical analyses on these figures were reported.

The incremental cost of Promogran plus GWC versus GWC alone was Euro 169 in France, Euro 283 in Germany, Euro 250 in Switzerland and Euro 1,079 in the UK.

No allowance was made for the cost of intervention-related adverse effects or knock-on costs.

Synthesis of costs and benefits
The costs and benefits were not synthesised as a cost-consequences analysis was conducted. The sensitivity analysis showed that Promogran was no longer cost-saving in France and Switzerland if a 50% lower relative efficacy of the intervention were used. The same occurred in France and Germany if the frequency at which the Promogran dressing
was changed was increased to 5 times per week.

**Authors' conclusions**
The treatment of diabetic non-superficial foot ulcers with Promogran in conjunction with good wound care (GWC) resulted in more healed ulcers and a shorter healing time than GWC alone. It was also a cheaper treatment option from the perspective of the health care provider.

**CRD COMMENTARY - Selection of comparators**
No explicit rationale for the choice of comparator was given in the paper. However, it appears to have been a valid alternative course of treatment. Readers should consider current treatment of non-superficial diabetic foot ulcers in their own setting before applying the results of this study in their own area.

**Validity of estimate of measure of effectiveness**
The evidence used to determine the effectiveness of the treatment was mainly drawn from other published studies. The papers do not seem to have been selected in a systematic manner and no quality criteria appear to have been applied. A systematic review of published studies would have provided a more robust estimate of the effectiveness of the intervention. The authors appear to have used the data from the primary studies selectively, as the majority of the data were derived from a single study. The strength of the estimate of effectiveness would have been enhanced by considering the differences in the results of the primary studies.

The data from the published studies were supplemented by the opinion of a Delphi panel of experts. The way in which the experts were chosen and the methods used to combine their views were not reported. This introduced a considerable degree of opaqueness to the methods of determining the effectiveness of the treatment. The authors highlighted the fact that the effectiveness data may not be generalisable to all four countries. Sensitivity analyses were undertaken on the parameters used in the model in an attempt to improve the external validity of the results. It should also be noted that the authors assumed that the Promogran dressing would be changed every 48 hours or 16 times a month, rather than every 24 or 36 hours as recommended by the manufacturers.

**Validity of estimate of measure of benefit**
No summary measure of benefit was used as a cost-consequences analysis was undertaken.

**Validity of estimate of costs**
The authors did not explicitly state the perspective from which the study was undertaken. However, it appears to have been conducted from the health care provider's prospective. This has been confirmed in recent correspondence with the authors. The study included the costs of inpatient stays, outpatient care and drugs. Consequently, the study seems to have included all the relevant costs. These costs were, appropriately, not discounted since the study period was only 12 months. The price year was reported, thus aiding reflation exercises.

In costing the Promogran dressings, the authors allowed for a new dressing to be applied every 48 hours despite the manufacturer's recommendation of every 24 to 36 hours. No explanation was given for this decision, which has the effect of underestimating the total cost of the intervention. The paper did not give specific details of the sources of the cost information for the treatment costs, other than for the Promogran dressing. This means that the method of calculation remains unclear. On a more positive note, the provision of a breakdown of the quantities and unit costs of the resources gives a clear format that can be used to compare studies.

**Other issues**
The authors did not compare their results with other studies, nor comment on how readily their findings could be generalised to other settings. However, a clear and comprehensive sensitivity analysis increased the external validity of the study.
Implications of the study
The authors did not make any specific recommendations in relation to changes to practice.

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Other publications of related interest

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