Cost-effectiveness comparison of therapy for psoriasis with a methotrexate-based regimen versus a rotation regimen of modified cyclosporine and methotrexate
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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
Two strategies for the treatment of psoriasis were studied. The strategies were methotrexate and a rotational schedule of modified cyclosporine (Neoral) with methotrexate.

Patients assigned to the methotrexate strategy received generic methotrexate (10 to 20 mg/week) with folic acid (1 mg/day). However, if the patient experienced a therapy failure under this regimen, their therapy was changed to receiving cyclosporine, alternating annually with the escape therapy, either until the end of the study or until the patient experienced a failure with cyclosporine (doses given below). In the case of such failure, the patient was assigned to the escape therapy for the remainder of the study.

If a patient assigned to the rotational strategy first experienced failure with methotrexate they were changed to a therapy of cyclosporine in rotation with the escape therapy for the remainder of the therapy or until cyclosporine failed, in which case the patient received the escape therapy for the remainder of the study.

Patients assigned to the rotational strategy alternated annually between receiving modified cyclosporine (Neoral) at a dose of 250 mg/day (3.0 - 3.5 mg/kg per day for patients weighing 71 - 84 kg) and methotrexate (dose as above). Patients continued on this rotation unless they experienced failure with one of the treatments. If patients experience treatment failure whilst receiving cyclosporine they were assigned to continuous therapy with methotrexate for the remainder of the study, or until failure with methotrexate occurred. In the case of failure with methotrexate, the patients were assigned to continuous treatment with the escape therapy until the end of the study.

The escape therapy was not a specific treatment. It represented alternative treatments that were assumed to provide no additional benefits, but to merely provide maintenance treatment for psoriasis.

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised patients with moderate to severe psoriasis. Inclusion and exclusion criteria were not reported.

Setting
The setting was not explicitly reported, but it would appear to have been primary care. The economic study was carried out in the USA.
Dates to which data relate
The years when the effectiveness and resource use data were collected were not reported. The price year for all costs was unclear. However, the authors stated that the cost of escape therapy was estimated from 1999 prices.

Source of effectiveness data
The effectiveness data were derived from a synthesis of published results. Where evidence was inconclusive or unavailable, expert opinion was sought.

Modelling
The course of the disease and the incidence of adverse events under different treatment strategies were modelled using decision trees with embedded Markov processes.

Outcomes assessed in the review
The outcomes assessed were changes in clinical status relating to the treatment strategies that were modelled.

Study designs and other criteria for inclusion in the review
The authors looked for evidence from randomised controlled trials. Other inclusion and exclusion criteria were not 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
Not reported.

Methods of combining primary studies
Not reported.

Investigation of differences between primary studies
Not reported.

Results of the review
The following effectiveness results were derived both from published material and from expert opinion. The results were presented according to clinical status (severe, moderate, mild, clear) at the end of that year.

The percentages of patients with severe psoriasis who had received methotrexate for one year were severe 8%, moderate 45%, mild 45%, and clear 2%.
The percentages of patients with moderate psoriasis who had received methotrexate for one year were severe 1%, moderate 10%, mild 86%, and clear 3%.

The percentages of patients with mild psoriasis who had received methotrexate for one year were severe 0%, moderate 1%, mild 96%, and clear 3%.

The percentages of patients with psoriasis categorised as clear, and who had received methotrexate for one year, were severe 0%, moderate 0%, mild 79%, and clear 21%.

The percentages of patients with severe psoriasis who had received cyclosporine for one year were severe 5%, moderate 10%, mild 45%, and clear 40%.

The percentages of patients with moderate psoriasis who had received cyclosporine for one year were severe 1%, moderate 3%, mild 36%, and clear 60%.

The percentages of patients with mild psoriasis who had received cyclosporine for one year were severe 0%, moderate 1%, mild 5%, and clear 94%.

The percentages of patients with psoriasis categorised as clear, and who had received cyclosporine for one year, were severe 0%, moderate 0%, mild 10%, and clear 90%.

**Methods used to derive estimates of effectiveness**

Expert opinion was used where evidence was inconclusive or unavailable.

**Estimates of effectiveness and key assumptions**

See the 'Results of the Review' section for summary estimates.

**Measure of benefits used in the economic analysis**

The measure of benefit used was the number of years clear of psoriasis.

**Direct costs**

The resource quantities and the costs were not reported separately. The direct costs included appear to have been those of the health service. The authors reported that only partial costs were included in the paper. These were for cyclosporine, methotrexate (with folic acid, escape therapy, complete blood cell count and platelet count, laboratory panel, creatinine clearance, liver biopsy (all costs), nifedipine for treating hypertension, and return visit physician fee (level 1, $10 per visit; level 3, $40 per visit; level 4, $75 per visit).

No rationale was given for the costs not documented in this paper. The costs were confirmed at retail with the University of Michigan Health System pharmacy. The total costs of therapy with psoralen and ultraviolet A corrected for 1999 dollars were used as a proxy for escape therapy for patients with a history of moderate or severe psoriasis. The authors reported that all the costs were calculated as University of Michigan Health System charges, modified by the Medicare cost-to-charge ratio. Discounting was relevant, as the model considered costs over a 10-year period, but there was no evidence that it had been undertaken. The study reported the average 10-year per-patient costs. The cost of escape therapy was estimated from 1999 prices. The price year for other costs was not stated explicitly.

**Statistical analysis of costs**

No statistical analysis of the costs was reported.

**Indirect Costs**

The indirect costs were not reported.
Currency
US dollars ($).

Sensitivity analysis
A sensitivity analysis around the costs and effectiveness was conducted. The area of uncertainty investigated was variability in the data. The rationale used to determine the ranges over which variables were tested was not documented in this paper. The authors did not report which method of sensitivity analysis was undertaken.

Estimated benefits used in the economic analysis
The results showed that patients receiving the cyclosporine strategy had approximately 4 years clear of psoriasis and 4 years with mild psoriasis. The methotrexate strategy resulted in approximately 2 years clear of psoriasis and 6.5 years of mild psoriasis. Both strategies were found to achieve similar results in terms of the number of years with moderate and severe psoriasis. The side effects of treatment were not considered in the economic analysis.

Cost results
Over 10 years, the total cost of the methotrexate strategy was $33,000 and that of the cyclosporine rotational strategy was $38,000.

It was found that the costs associated with liver biopsy were slightly lower under the cyclosporine strategy, in which patients took fewer years of methotrexate.

The cost of treating side effects was $678 under the cyclosporine strategy and $324 under the methotrexate strategy. These costs represented less than 2% of the total cost.

The authors reported that, if the cost of cyclosporine was approximately $100 per month, the methotrexate and cyclosporine strategies would be equal in cost.

Synthesis of costs and benefits
The benefits and costs were combined by estimating the cost per year free of psoriasis. An incremental analysis was performed. It was calculated that, for the cyclosporine strategy, the base-case cost-effectiveness ratio was $2,700 per incremental year clear of psoriasis. Further, when the relative effectiveness of cyclosporine to produce a year of clear skin was varied over a range of approximately 1 to 20 times the effectiveness of methotrexate, the cost-effectiveness ratio ranged from more than $4,100 to approximately $2,700 per incremental year clear.

Authors' conclusions
The simulation indicated that the treatment of patients with severe and moderate psoriasis over a 10-year period with the cyclosporine rotational strategy provided additional clinical benefits over the methotrexate strategy, at approximately 15% greater expense.

CRD COMMENTARY - Selection of comparators
The authors explained that the comparator was chosen because it has often been considered the "gold" standard, having been used in the treatment of severe psoriasis for 40 years. You should decide if this is a widely used health technology in your own setting.

Validity of estimate of measure of effectiveness
The authors did not state that a systematic review of the literature had been undertaken. Since they did not report the method used to derive estimates of effectiveness from the primary studies, it is unclear whether the effectiveness
measures were used selectively or whether the derived measures were combined. A lack of reported detail makes it impossible to comment on the impact of differences between the primary studies when estimating effectiveness. The methods used to derive measures of effectiveness from expert opinion were not reported. Estimates of the relative effectiveness of methotrexate and cyclosporine in producing improvement and clearance were investigated in a sensitivity analysis. The ranges used appear to have been wide.

**Validity of estimate of measure of benefit**
The estimation of benefits was obtained directly from the effectiveness analysis. This estimate was chosen as the primary outcome measure because studies had shown that patients highly value the clearing of psoriasis lesions.

**Validity of estimate of costs**
The authors only reported a partial list of cost inputs, so it is not possible to comment on whether all the categories of cost and the costs relevant to each category have been included in the study, or whether any omissions are likely to have affected the authors’ conclusions. The costs and the quantities were not reported separately. Some quantities appear to have been taken from published sources, whereas the sources of other quantities were unclear. A sensitivity analysis of the quantities was not conducted. It is possible that this may limit the interpretation of the study findings. Prices were taken from published sources. A sensitivity analysis of the prices was not conducted. Discounting was not undertaken even though the costs were incurred during a 10-year period. It does not appear that charges were used to proxy costs. The date to which the prices related was unclear.

**Other issues**
The authors made appropriate comparisons of their findings with those from other studies. However, the issue of the generalisability to other settings was not addressed. Although only few results were reported, the authors do not appear to have presented their results selectively and their conclusions reflected the scope of the analysis. The authors reported further limitations to their study. First, they acknowledged the difficulties inherent in creating a model that exactly reflects patient and physician choices. Second, there was a lack of data on the effectiveness, incidence of side effects and costs of treatment strategies (particularly for methotrexate therapy). Finally, there was an absence of indirect costs and quality of life measures from the study.

**Implications of the study**
The authors suggested that the findings from the study should be used when contemplating treatment and reimbursement decisions for patients with moderate to severe psoriasis.

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