Cost effectiveness of imiquimod 5% cream compared with methyl aminolevulinate-based photodynamic therapy in the treatment of non-hyperkeratotic, non-hypertrophic actinic (solar) keratoses: a decision tree model

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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.

CRD summary
This study assessed the cost-effectiveness of imiquimod versus photodynamic therapy (PDT) for the treatment of solar or actinic keratosis of the face and scalp, in patients with four to nine lesions, who were unsuitable for cryosurgery, topical diclofenac, and topical fluorouracil. The author concluded that PDT was unlikely to be cost-effective compared with imiquimod and a head-to-head trial was needed. The methods were robust and transparently presented. The author's conclusions appear to be valid.

Type of economic evaluation
Cost-utility analysis

Study objective
This study assessed the cost-effectiveness of imiquimod versus photodynamic therapy (PDT) for the treatment of solar or actinic keratosis of the face and scalp, in patients with four to nine lesions, who were unsuitable for cryosurgery, topical diclofenac, and topical fluorouracil.

Interventions
The interventions were imiquimod 5% cream and PDT using methyl aminolevulinate. Imiquimod cream was applied to the face and scalp once daily and left on for eight hours. This was repeated three times per week for four weeks and followed by four weeks without treatment. PDT was repeated after 12 weeks if unsuccessful.

Location/setting
UK/secondary care.

Methods
Analytical approach:
The analysis was based on a decision-tree model, with a one-year horizon. The author stated that the perspective was that of the third-party payer, which was the UK NHS.

Effectiveness data:
The clinical data were from a literature review in PubMed and the Cochrane Library. The numbers of studies identified and selected were reported in an online appendix, with the key characteristics of each study. The treatment effect (baseline risk and relative risk) was mainly from randomised controlled trials. A meta-analysis was performed, using the inverse variance method, to pool the evidence from the selected studies. No head-to-head studies were found and an indirect comparison was needed. The adverse event information was from clinical trials. The response rates were the key input for the model.

Monetary benefit and utility valuations:
The utility values were from studies found in the PubMed database. The estimates for patients with actinic keratosis were from a study that used the standard gamble technique and a study that used the time trade-off method. The disutilities associated with adverse events were from studies of patients with conditions of similar severity.

Measure of benefit:
Quality-adjusted life-years (QALYs) were the summary benefit measure.

**Cost data:**
The economic analysis included the costs of imiquimod, PDT, and out-patient consultations (initial and follow-up visits and treatment for adverse events). The unit costs were from NHS reference costs and the British National Formulary. The resource quantities were based on a conventional treatment protocol. A specific cost for PDT was not identified and the cost of laser destruction of skin lesions was used. All costs were in UK pounds sterling (£) and the price year was 2006.

**Analysis of uncertainty:**
A probabilistic sensitivity analysis was undertaken, using 5,000 Monte Carlo simulations and conventional probability distributions for the model inputs. Cost-effectiveness acceptability curves were created. One-way sensitivity analyses were conducted on selected inputs.

**Results**
The expected one-year costs were £360 with imiquimod and £534 with PDT. The QALYs were 0.983 with imiquimod and 0.988 with PDT. The incremental cost per QALY gained with PDT over imiquimod was £34,576, which was above the cost-effectiveness thresholds of £20,000 or 30,000 per QALY.

There was a 75% chance of imiquimod being cost-effective, compared with PDT, at a threshold of £20,000 per QALY and a 73% chance at £30,000 per QALY.

These results were affected by changes in the key inputs. For example, imiquimod was no longer cost-effective at £30,000 per QALY when the risk of adverse events with imiquimod was over 60% (base case 53%) or when the cost of PDT was under £225 (base case £270).

**Authors’ conclusions**
The author concluded that imiquimod and PDT had similar costs and effectiveness, but PDT was unlikely to be cost-effective compared with imiquimod. A direct head-to-head study was required to establish the relative response rates.

**CRD commentary**

**Interventions:**
The rationale for the selection of the comparators was clear as they were the available treatments for these patients, for whom other options were unsuitable. The two interventions were described.

**Effectiveness/benefits:**
A valid approach was used to identify the clinical data sources. Extensive details of the literature review and the methods used to extract and combine the evidence were reported. Clinical trials were used for the treatment effect and the absolute baseline risk, and they are likely to have had high internal validity. They were described in the online appendix and their comparability was investigated. An indirect comparison was required because of the lack of head-to-head trials. Extensive sensitivity analysis was performed on the key clinical parameters. QALYs were a valid benefit measure for capturing the impact of the disease on health and they allow comparisons with the benefits of other health care interventions. The methods used to elicit the preferences were appropriate and commonly used.

**Costs:**
The economic analysis was satisfactorily carried out. The unit costs and resource quantities were presented for most items. The cost categories and their sources were consistent with the perspective of the third-party payer and they were representative of the UK. Reflation exercises will be possible as the price year was clearly stated. Alternative cost estimates were tested in the sensitivity analyses and the costs were varied in the probabilistic analysis.

**Analysis and results:**
The results were clearly reported. Both total and incremental figures were presented. An incremental approach was used to synthesise the costs and benefits of the two strategies. Appropriate tools were used to investigate uncertainty and the results were clearly illustrated and discussed. The author justified the choice of decision model and the time horizon.
which were appropriate to simulate disease management and to capture all the relevant outcomes. A comparison with other published economic evaluations was made and there were differences in assumptions or methods. The generalisability of the results was not discussed, but the findings could be transferred to settings with similar health care costs.

Concluding remarks:
The methods were robust and transparently presented. The author’s conclusions appear to be valid.

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