An economic evaluation of topical treatments for actinic keratosis
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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 aimed to assess the cost-effectiveness of the topical treatments 5-fluorouracil and imiquimod, as well as photodynamic therapy using methyl aminolevulinate, for the treatment of patients with actinic keratosis. The authors concluded that the costs and effectiveness of photodynamic therapy in the UK NHS compared well with those of the other treatments, but head-to-head clinical trials would be useful. There appears to be too much uncertainty around the validity of the clinical evidence to be confident in these conclusions.

Type of economic evaluation
Cost-effectiveness analysis

Study objective
The aim was to assess the cost-effectiveness of topical treatments, such as 5-fluorouracil and imiquimod, as well as photodynamic therapy using methyl aminolevulinate, for the treatment of patients with actinic keratosis.

Interventions
The interventions were first-line treatment with 5-fluorouracil for four weeks; imiquimod three times a week for four weeks, followed by no treatment for four weeks, then another four-week course if the lesions remain; and one or two sessions of methyl aminolevulinate and photodynamic therapy. Cryotherapy, diclofenac, curettage, electrosurgery, and excision were the possible second-line treatments in the model.

Location/setting
UK/secondary care.

Methods
Analytical approach:
A decision analytic model was used to combine the effectiveness and cost data from a variety of sources. The model explored the costs and outcomes for two lines of treatment. The time horizon was up to two lines of treatment, each lasting a maximum of one year. The expert opinion of seven clinicians was elicited to determine the choice of second-line treatment after the failure of each initial treatment; these data were reported in a table. The authors stated that the analysis took the perspective of the UK NHS.

Effectiveness data:
A literature review was conducted to identify published estimates of the effectiveness of each treatment. The main clinical parameters were the probability of complete response to treatment and the probability of an excellent cosmetic outcome, given a complete response. These data came from different trials for each treatment. The proportion of patients with each outcome in each treatment arm from these trials was reported.

Monetary benefit and utility valuations:
Not relevant.

Measure of benefit:
The primary measure of benefit was the proportion of patients achieving an excellent cosmetic outcome after a complete response.

Cost data:
The cost categories included: drugs, dermatologist consultations, and second-line treatments, including resurfacing, cryotherapy, imiquimod, 5-fluorouracil, plastic surgery consultations, and plastic and reconstructive surgery. The capital cost of the photodynamic therapy equipment was not included as it was not directly paid by the NHS. The drug dosages were assumed based on manufacturer recommendations and authors’ assumptions. Photodynamic therapy was based on Belgian data. The number of consultations and frequency of second-line treatments were from the survey of seven clinicians. The drug costs were from the British National Formulary. Other unit costs were from standard sources. The costs were reported in 2007 UK pounds sterling (£), inflated using NHS inflation rates.

Analysis of uncertainty:
One-way and probabilistic sensitivity analyses were conducted. One-way sensitivity analysis was conducted on the rate of excellent cosmetic outcome following complete response, for patients treated with imiquimod and 5% 5-fluorouracil. The same rate as for photodynamic therapy (83.1%) was used, and the midpoint between the rate observed with cryotherapy and that with photodynamic therapy (67.0%) was used. Probabilistic sensitivity analysis, with 1,000 simulations, was conducted on the clinical effectiveness, using beta distributions, and the costs, using log-normal distributions.

Results
The total cost of treatment was £436.83 with two lines of photodynamic therapy, £418.23 with photodynamic therapy then various second-line treatments, £480.55 with imiquimod, and £366.75 with 5-fluorouracil.

The percentage of patients achieving a complete response was 88.6% with two lines of photodynamic therapy, 91.7% with photodynamic therapy then various second-line treatments, 86.6% with imiquimod, and 89.0% with 5-fluorouracil.

The percentage of patients achieving an excellent cosmetic outcome was 73.6% with two lines of photodynamic therapy, 73.1% with photodynamic therapy then various second-line treatments, 49.6% with imiquimod, and 49.7% with 5-fluorouracil.

The incremental cost per additional patient with a complete clinical response and an excellent cosmetic outcome was £220 for photodynamic therapy then various second-line treatments, compared with 5-fluorouracil.

The probabilistic sensitivity analysis revealed that photodynamic therapy then various second-line treatments dominated (was more effective and cheaper than) two lines of photodynamic therapy in 89% of simulations, imiquimod in 99% of simulations, and 5-fluorouracil in 3% of simulations, in terms of complete clinical response; and in 43% for two lines, 99% for imiquimod, and 3% for 5-fluorouracil, in terms of excellent cosmetic outcome.

Authors’ conclusions
The authors concluded that the costs and effectiveness of photodynamic therapy in the UK NHS compared well with those of the other treatments for actinic keratosis, but head-to-head clinical trials could confirm this.

CRD commentary
Interventions:
The first-line treatments were well described, but less information was provided on the second-line treatments. The authors mentioned different categories of treatment, but only analysed topical treatments. It is possible that other treatments are more cost-effective.

Effectiveness/benefits:
The estimates of treatment efficacy were well reported. The details of the literature review were not provided and so it is unclear whether it was a systematic review and thus whether all the relevant sources of efficacy were found. The authors reported the percentages of patients achieving the specific outcome in the individual trial arms, suggesting that they assumed equal populations and protocols across trials and trial arms, ignoring the benefits of randomisation. If this was the case, there was considerable potential for bias. The authors acknowledged the need for further evidence. No discounting was applied due to the short time horizon.

Costs:
The quantities and prices of the creams were reported. The cost categories were appropriate for the perspective. The price year, currency, and adjustments to the costs were reported. The authors noted the limitation that they had to rely on questionnaires from seven clinicians. No discounting was applied due to the short time horizon.

Analysis and results:
The use of a decision analytic model was appropriate for synthesising the data from a variety of sources. The reporting of the results as the cost per complete treatment response and the cost per excellent cosmetic outcome was appropriate, but these measures did not fully consider the quality of life. One-way sensitivity analyses and probabilistic sensitivity analyses were performed, but it was not clear which values were tested and what alternative assumptions were made. A probabilistic analysis will only assess the overall uncertainty if the ranges of values tested are sufficiently wide and all parameters are varied. The authors noted several limitations to their analysis.

Concluding remarks:
There appears to be too much uncertainty around the validity of the clinical evidence to be confident in the conclusions.

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