Economic evaluation of methyl aminolaevulinate-based photodynamic therapy in the management of actinic keratosis and basal cell carcinoma

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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 methyl aminolaevulinate-based photodynamic therapy (MAL-PDT) for the treatment of both actinic keratosis (AK) and basal cell carcinoma (BCC). MAL-PDT is a 160 mg/g cream which is usually given in combination with red light.

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised a cohort of patients with AK and BCC. Specifically, the study target population in the AK analysis included patients with AK lesions larger than 5 mm in diameter on the face or scalp. The target population in the BCC analysis included patients with primary nodular BCC (nBCC) lesions suitable for simple excision surgery and patients with superficial BCC (sBCC) lesions suitable for cryotherapy. "This means nBCC and sBCC in the H-zone (around the eyes or near the nasolabial or retroauricular folds), or patients with a large sBCC or nBCC lesion not in the H-zone."

Setting
The setting was a hospital. The economic study was carried out in Belgium.

Dates to which data relate
The effectiveness data were derived from studies published between 1989 and 2004. No dates for the resource use were reported, as this was based on expert opinion. The price year was 2002.

Source of effectiveness data
The effectiveness evidence was derived from a synthesis of published studies.

Modelling
A decision tree was constructed to simulate the clinical and economic consequences of the use of MAL-PDT, compared with cryotherapy for AK and excision surgery for BCC, in a hypothetical cohort of eligible patients. The time horizon was 1 year for AK patients and 5 years for BCC patients. The model for AK consisted of initial management (MAL-PDT or cryotherapy), second-line management and follow-up cosmetic assessment. After initial management, patients could have a full clinical response or not. In the latter case, the remaining lesions received second-line treatment. In patients in whom all lesions were cured, the cosmetic outcome could be excellent or non-excellent. For patients with a
non-excellent cosmetic outcome, additional interventions such as reconstructive surgery, or treatment of pigment anomalies with creams, were considered. The model for BCC was similar to the AK model, but other second-line options were considered. In addition, patients with full response after the initial management (MAL-PDT or excision surgery) could have a recurrence. Further, a distinction was made between primary nBCC and sBCC, given the different clinical outcomes. The structures of the two decision models were reported graphically.

**Outcomes assessed in the review**
The outcomes estimated from the literature were:

- the initial rates of patients with all lesions responding to the treatments investigated (MAL-PDT or cryotherapy for AK, MAL-PDT or excision surgery for nBCC and sBCC);
- the probability of excellent cosmetic outcome (defined as absence of scarring, atrophy or induration, and no or slight occurrence of redness or change in pigmentation compared with adjacent skin) for all treatments analysed; and
- the recurrence rate (with MAL-PDT or excision surgery for nBCC and sBCC).

**Study designs and other criteria for inclusion in the review**
It was not stated whether the primary studies were identified through a systematic review of the literature. Clinical data on treatment efficacy came from three large, international, clinical trials. Each trial provided efficacy data based on direct comparisons for the treatments analysed. Some information on the sample size was reported for each trial. No information on the other sources of data was provided.

**Sources searched to identify primary studies**
Not reported.

**Criteria used to ensure the validity of primary studies**
The validity of the primary estimates was ensured by the use of clinical trials.

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

**Number of primary studies included**
Six primary studies provided the clinical data.

**Methods of combining primary studies**
Each study provided a specific clinical outcome, thus the primary studies were not combined.

**Investigation of differences between primary studies**
Not reported.

**Results of the review**
In AK patients, the initial rate of full responders was 80.7% with MAL-PDT and 57.3% with cryotherapy.

In nBCC patients, the initial probability of full responders was 86.5% with MAL-PDT and 93.9% with surgical excision.
In sBCC patients, the initial probability of full responders was 88.7% with MAL-PDT and 94.9% with surgical excision.

In AK patients, the probability of an excellent cosmetic result was 83% with MAL-PDT and 51% with cryotherapy.

In BCC patients, the probability of an excellent cosmetic result was 43% with MAL-PDT and 7% with surgical excision.

In BCC patients, the recurrence rate was 11% (over a 3-year period) with MAL-PDT and 10.1% (over a 5-year period) with surgical excision.

The 3-year recurrence rate for BCC patients with MAL-PDT was linearly extrapolated over 5 years, giving a 5-year recurrence rate of 18.3%.

**Measure of benefits used in the economic analysis**
The summary benefit measure was the probability of full responders over the relevant time horizon. Full responders were defined as patients with clinically responding lesions and an excellent cosmetic result. An annual rate of 3% was used to discount benefits to present values for the 5-year analysis (only BCC).

**Direct costs**
The analysis of the costs was undertaken from the viewpoint of the public health insurance. It included the costs associated with the procedures under examination, medical visits, diagnostic tests and drugs. A detailed breakdown of the cost items was not provided. The unit costs were not presented separately from the quantities of resources used for most items, and only the total costs were provided. Resource use was derived from a Delphi panel comprising a sample of 12 Belgian dermatologists who participated in a two-round process. The costs were obtained from the official listings of the Belgian Health Insurance. Details of how the cost of MAL-PDT was calculated were reported. Discounting was relevant in the BCC model, given the 5-year time horizon, and an annual rate of 3% was used. The price year was 2002.

**Statistical analysis of costs**
A triangular distribution was assigned to costs in the probabilistic sensitivity analysis.

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

**Currency**
Euros (EUR).

**Sensitivity analysis**
A probabilistic sensitivity analysis was carried out to define potential ranges of costs and cost-effectiveness ratios. All model inputs were assigned a probabilistic distribution (binomial for probabilities, triangular for resource use and costs).

**Estimated benefits used in the economic analysis**
In the AK model, the expected probability of full response was 0.729 with MAL-PDT and 0.424 with cryotherapy.

In the nBCC model, the expected probability of full response was 0.3315 with MAL-PDT and 0.0738 with surgical excision.

In the sBCC model, the expected probability of full response was 0.3377 with MAL-PDT and 0.0737 with surgical excision.
excision.

Cost results
In the AK model, the expected costs were EUR 277.30 (range: 267.10 to 289.30) with MAL-PDT and EUR 152.90 (range: 134.40 to 170.70) with cryotherapy.

In the nBCC model, the expected costs were EUR 402.80 (range: 382.00 to 423.10) with MAL-PDT and EUR 280.70 (range: 251.00 to 309.10) with surgical excision.

In the sBCC model, the expected costs were EUR 345.20 (range: 326.90 to 367.20) with MAL-PDT and EUR 278.30 (range: 248.40 to 307.30) with surgical excision.

Synthesis of costs and benefits
An incremental cost-effectiveness ratio (ICER; i.e. the incremental cost per full responder) was calculated in order to combine the costs and benefits of the alternative strategies.

The ICER associated with MAL-PDT over the relevant comparator was EUR 401.10 (range: 290.40 to 596.50) in the AK model, EUR 468.60 (range: 325.60 to 715.50) in the nBCC model, and EUR 251.20 (range: 143.70 to 422.00) in the sBCC model.

Authors' conclusions
The use of methyl aminolaevulinate-based photodynamic therapy (MAL-PDT) to treat patients with actinic keratoses (AK) or basal cell carcinoma (BCC) was a cost-effective strategy in comparison with other currently used treatments such as cryosurgery (as an alternative for AK patients) or surgical excision (as an alternative for BCC patients) in Belgium. Society's willingness to pay for one day of response may represent a key issue for the choice of MAL-PDT in AK patients.

CRD COMMENTARY - Selection of comparators
The authors justified their choice of the comparators, which represented the most commonly used treatments among those available for patients with AK or BCC in Belgium. Radiotherapy was not chosen as a comparator to MAL-PDT for the treatment of BCC because its position in the treatment of BCC has been questioned and it is no longer frequently used in Belgium. You should decide whether they are valid comparators in your own setting.

Validity of estimate of measure of effectiveness
The effectiveness data were derived from published studies. However, the authors did not explicitly report the methods and conduct of a systematic review of the literature, thus the primary studies might have been identified selectively. Much of the evidence came from clinical trials, which should have ensured a high internal validity of the primary data. Moreover, each study was based on direct comparison of the treatments analysed. The impact of variations in the clinical estimates was investigated in the probabilistic sensitivity analysis, but ranges around mean estimates were not reported.

Validity of estimate of measure of benefit
The summary measure of benefit was a disease-specific measure. This was appropriate given that it took response to treatment and cosmetic outcomes, which represent two relevant aspects for patients with either AK or BCC, into account. However, the use of a specific measure has the disadvantage that it cannot be directly compared with the benefits of other health care interventions. The assessment of the impact of the interventions on quality of life would have been interesting, as the authors pointed out, not only in terms of capturing all relevant aspects of health but also in permitting comparisons with other interventions.
Validity of estimate of costs
The authors explicitly stated the perspective chosen for the analysis and the cost categories included in the study were consistent with that choice. A detailed breakdown of the cost items was not provided, and, except for the cost of MAL-PDT, information on the unit costs and quantities of resources was not reported. This limits the possibility of replicating the analysis in other settings. The source of the costs was consistent with the viewpoint of the analysis. Resource use was based on expert opinion and should reflect actual treatment patterns in Belgium. Discounting was relevant and was performed appropriately. The impact of individual cost items on the total costs was not evaluated, but the issue of variability of the costs was addressed in global terms in the probabilistic sensitivity analysis. The authors reported the price year, which will help in reflating costs estimates in other time periods.

Other issues
The authors did not compare their findings with those from other studies. It was stated that the issue of uncertainty was extensively addressed in the probabilistic sensitivity analysis, especially with respect to cost estimates. However, the issue of the generalisability of the study results to other settings was not explicitly addressed. The study referred to patients with AK or BCC and this was reflected in the authors’ conclusions. The results of the analysis were clearly presented. However, a key issue in understanding the cost-effectiveness of MAL-PDT appears to be the real willingness to pay for a patient fully responding to BCC and AK treatments.

Implications of the study
The authors suggest that MAL-PDT should be adopted for the treatment of AK and BCC if society is willing to pay for it. They also recommend that quality of life data be collected to measure health outcomes. It would also be informative if outcomes for AK were to be measured over a longer time horizon.

Source of funding
None stated.

Bibliographic details

PubMedID
16965429

DOI
10.1111/j.1365-2133.2006.07483.x

Other publications of related interest
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**Indexing Status**
Subject indexing assigned by NLM

**MeSH**
Aminolevulinic Acid / analogs & derivatives / economics / therapeutic use; Belgium; Carcinoma, Basal Cell / drug therapy / economics / surgery; Cost-Benefit Analysis; Cryosurgery / economics; Decision Making; Drug Costs / statistics & numerical data; Health Care Costs / statistics & numerical data; Humans; Keratosis / drug therapy / economics / surgery; Models, Econometric; Photochemotherapy / economics / methods; Photosensitizing Agents / economics / therapeutic use; Skin Neoplasms / drug therapy / economics / surgery

**Accession Number**
22006001822

**Date bibliographic record published**
28/02/2007

**Date abstract record published**
28/02/2007