Cost-effectiveness of Mohs micrographic surgery vs surgical excision for basal cell carcinoma of the face

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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 study examined two surgical treatments for both primary and recurrent basal cell carcinoma (BCC) of the face. The treatments were Mohs micrographic surgery (MMS) and surgical excision (SE).

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised patients with a primary or recurrent BCC of the face. In particular, eligible patients with a primary BCC were those with a histologically proven tumour larger than 1 cm located in the H-zone of the face, or an aggressive histopathologic sub-type. Eligible patients with a recurrent BCC were first- and second-time cases. Patients with a life expectancy of less than 3 years, based on expert opinion of the dermatologist, were excluded.

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

Dates to which data relate
The effectiveness data and most resource use data were derived from a study published in 2004, in which 1999 to 2002 data were used. The price year was 2001.

Source of effectiveness data
The effectiveness evidence was derived from a single study.

Link between effectiveness and cost data
The costing was carried out prospectively on the same sample of patients as that used in the analysis of effectiveness.

Study sample
Power calculations were performed in the preliminary phase of the study. These showed that the clinical trial was designed to have a 90% power to detect a 6.5% difference in the recurrence rate between MMS and SE for primary BCC, and a 13.5% difference for recurrent BCC at the 5% level of significance. A total of 408 primary (374 patients) cases of facial BCC were included in the study. Of these, 204 were in the SE group and 204 in the MMS group. The mean age was 67.7 (+/- 12.7) years and 60% were male. There were 204 recurrent cases of facial BCC (191 patients) in
the study. Of these, 102 were in the SE group and 102 in the MMS group. The mean age was 67.9 (+/- 11.7) years and 58% were male. Patients with more than one BCC were included multiple times.

Study design
This was a prospective, randomised clinical trial that was carried out at a single centre, the dermatology outpatient clinic of the University Hospital Maastricht. Separate randomisation procedures were performed for both primary and recurrent BCC. The length of follow-up was 30 months for the primary BCC sample and 18 months for the recurrent BCC sample. In the group of primary BCC, 33 patients (16%) in the SE group and 44 patients (22%) in the MMS group were lost to follow-up. In the group of recurrent BCC, 9 patients (9%) in the SE group and 7 patients (7%) in the MMS group were lost to follow-up. Blinding does not appear to have been performed.

Analysis of effectiveness
The analysis of the clinical study was based on modified intention to treat in which missing cases were excluded. The primary outcome measure was the recurrence of a BCC for both samples of patients. The secondary outcome measures were frequency of complications, quality of life and anxiety. Quality of life and anxiety were estimated using two tools, the Dutch version of the Nottingham Health Profile (NHP) and a domain-specific questionnaire (the Dutch version of the State-Trait Anxiety Inventory, STAI). Both instruments were administered at baseline and after 6 months. The authors did not state whether the study groups had comparable clinical and demographic factors at baseline, but the groups were likely to have been similar given the randomisation process.

Effectiveness results
In the primary BCC sample, there were 5 recurrences in the SE group and 3 in the MMS group at 30 months’ follow-up.

In the recurrent BCC sample, there were 3 recurrences in the SE group and 0 in the MMS group at 18 months’ follow-up.

In the primary BCC sample, there were 28 (14%) complications in the SE group and 24 (12%) in the MMS group.

In the recurrent BCC sample, there were 19 (19%) recurrences in the SE group and 8 (8%) in the MMS group, (p=0.02).

Mean scores for anxiety and quality of life were not statistically different between the groups.

Clinical conclusions
The effectiveness analysis showed that fewer recurrences and fewer complications were observed among patients undergoing MMS in comparison with those undergoing SE.

Measure of benefits used in the economic analysis
The summary benefit measure was the difference in recurrence rate between the groups. This was derived directly from the effectiveness analysis. An annual discount rate of 4% was applied.

Direct costs
The analysis of the costs was conducted from the viewpoint of the hospital. The categories of costs included were personnel and material costs of all diagnostic procedures, surgery, outpatient visits and overheads. Some unit costs were presented separately from the quantities of resources used. Resource use was based on actual resource consumption in the sample of patients included in the clinical trial, using a micro-costing approach. The costs were estimated from the authors’ institution and from Dutch guidelines. Discounting was relevant, as the costs were incurred during 30 months, and an annual rate of 4% was applied to costs incurred after the second year. The price year was 2001.
Statistical analysis of costs
The costs were analysed by the intention to treat principle with mean substitution of missing values. Regression analysis was performed to investigate the effect of location and histopathologic sub-type on the cost-difference between the groups. If non-normal distributions were present, log-transformation of the costs was applied. The bootstrap method was used to determine confidence intervals (CIs).

Indirect Costs
The indirect costs were not included in the economic analysis.

Currency
Euros (EUR). The exchange rate from euros to US dollars ($) and UK pounds sterling () in 2001 was EUR 1 = $0.89 = 0.69.

Sensitivity analysis
Univariate sensitivity analyses were carried out to assess the robustness of cost-effectiveness ratios to variations in personnel costs, effect difference between groups, and actual recurrence rates. Alternative published values, as well as authors' opinions, were used. Bootstrapping with 1,000 replications was performed to define CIs around the cost-effectiveness ratios. Subsequently, acceptability curves were generated for different threshold values.

Estimated benefits used in the economic analysis
In the sample of primary BCC, the expected rate of recurrence avoided was 0.9812 with MMS and 0.9725 with SE (difference 0.0091).

In the sample of recurrent BCC, the expected rate of recurrence avoided was 1.000 with MMS and 0.968 with SE (difference 0.032).

Cost results
In the sample of primary BCC, the expected costs were EUR 1,132 with MMS and EUR 866 with SE (difference EUR 266).

In the sample of recurrent BCC, the expected costs were EUR 1,159 with MMS and EUR 900 with SE (difference EUR 259).

Different in costs reached statistical significance in both the primary and recurrence BCC groups.

The higher costs associated with MMS were mainly due to the personnel costs arising from longer theatre time.

The regression analysis showed that location and histopathologic sub-type had no effect on the cost-difference between the groups.

Synthesis of costs and benefits
Incremental cost-effectiveness ratios (ICERs) were calculated in order to combine the costs and benefits of the alternative treatments.

The incremental cost per recurrence avoided with MMS over SE was EUR 29,231 in the sample of primary BCC and EUR 8,094 in the sample of recurrent BCC.

The most interesting results of the univariate sensitivity analysis were that substantial reductions in the ICER could be achieved when a larger difference in treatment effectiveness between groups was considered. Also, a longer follow-up period (5 years) substantially reduced the ICER (e.g. this was EUR 4,047 for the recurrence BCC group).
The acceptability curve showed that, for primary BCC, the probability of MMS being cost-effective for the calculated ICER of EUR 29,231 was 40%. For recurrent BCC, the probability of MMS being cost-effective for an ICER of EUR 8,094 was 30%.

Authors' conclusions
Mohs micrographic surgery (MMS) was an effective treatment for facial BCC in the Netherlands. However, due to the high cost of the technology, MMS was not cost-effective in comparison with surgical excision (SE), especially in patients with primary basal cell carcinoma (BCC).

CRD COMMENTARY - Selection of comparators
The rationale for the choice of the comparators was reported and was appropriate, given the objective of the study. MMS and SE were the most commonly used treatments for the treatment of both primary and recurrent BCC. You should decide whether they are valid comparators in your own setting.

Validity of estimate of measure of effectiveness
The effectiveness analysis was based on a clinical trial, which was appropriate for the study question. In addition, the use of a randomised design should have reduced the impact of selection bias. The methods of randomisation and sample selection were not described as further information on the clinical trial was reported in the primary publication. It was not stated whether some patients refused to participate or were excluded for any reasons from the initial study sample. Similarly, the baseline comparability of the study groups was not discussed. The use of a modified intention to treat analysis and the appropriateness of the study sample, which was justified on the basis of statistical analyses, represented two strong features of the analysis. Patients were enrolled at a single institution, which might reduce the representativeness of the patient population. Sensitivity analyses were performed in which the effectiveness results were varied. This appears to have been the variable with the highest impact on the cost-effectiveness results.

Validity of estimate of measure of benefit
The effectiveness measure was specific to the disease considered in the study, thus it will not be comparable with the benefits of other health care interventions. A quality adjustment was not considered since differences in quality of life were not observed between the groups. Similarly, the impact of the interventions on life expectancy was not investigated as the disease was not life-threatening.

Validity of estimate of costs
The analysis of the costs reflected the perspective of the health care provider and the cost categories included were appropriate. The authors justified the exclusion of some of the costs, such as indirect costs and out-of-pocket expenses. The unit costs and quantities of resources used were provided for most items, which enhances the possibility of replicating the analysis in other settings. The source of the data was reported for all items. Statistical analyses of the costs were carried out, and the impact of changing some key cost items was investigated in a sensitivity analysis. The price year was given, thus enhancing the possibility of reflating the costs in different time periods.

Other issues
The authors did not make extensive comparisons of their findings with those from other studies, but this was understandable given the lack of published cost-effectiveness studies on treatments for BCC. The issue of the generalisability of the study results to other settings was not explicitly addressed, but the use of sensitivity analyses on the most relevant data improved the external validity of the analysis. The study referred to patients with facial BCC and this was reflected in the authors' conclusions.

Implications of the study
The study results do not support the use of MMS for the treatment of patients with facial BCC, owing to the small
improvement in efficacy in comparison with SE and the high cost of the procedure.

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