Cost-utility analysis of high-dose melphalan with autologous blood stem cell support vs. melphalan plus prednisone in patients younger than 60 years with multiple myeloma

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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 health technology considered in the study was an intensive treatment with the high-dose melphalan (HDM) combined with autologous blood stem cell support (ABSCS) in patients under 60 years of age with multiple myeloma.

Type of intervention
Treatment.

Economic study type
Cost-utility analysis.

Study population
The study population comprised newly diagnosed, symptomatic myeloma patients under the age of 60.

Setting
The setting was the community. The economic study was carried out in Norway, Denmark, and Sweden.

Dates to which data relate
Data on effectiveness and the resources used were collected between March 1994 and July 1997. The price year was 2000.

Source of effectiveness data
The effectiveness evidence was based on a single study.

Link between effectiveness and cost data
The costing was undertaken prospectively on the same patient sample as that used in the effectiveness analysis.

Study sample
The sample size was not based on power calculations. Overall, 344 patients were considered: 274 patients (median age 51 years, 35% female) treated with the intensive therapy and 70 patients (median age 54 years, 44% female) with the conventional therapy. Eligibility criteria were not reported. Patients in the intensive therapy group were identified from a population-based trial (NMSG 5/94). Patients in the control group were selected retrospectively from five completed prospective studies: a cohort of 274 subjects was initially identified. From that control group 70 patients were randomised to treatment with MP.
Study design
The study was a population-based non-randomised multi-centre trial (NMSG 5/94) carried out in 14 regions in Denmark, Norway and Sweden. The control group was based on historical prospective studies. The duration of follow-up was not explicitly reported. However, since costs over 36 months were included, the authors used a survival curve to estimate the number of patients alive, and assumed that resource consumption per patient in the first and second year after the observation period for that patient was the same as the observed average consumption in a corresponding survival time period for other patients.

Analysis of effectiveness
The analysis of the clinical study was based on intention to treat. The primary health outcomes used in the analysis were the mean survival between the two groups and the quality of life estimated using EORTC QLQ-30 (version 1) questionnaires and HRQoL. Questionnaires were administered to patients in both groups prior to treatment and at regular intervals during the follow-up period. Many details about the clinical study (comparability of groups, adjustments for confounding factors, etc.) were reported in another paper.

Effectiveness results
Median survival was 62 months in the intensive treatment group and 44 months in the conventional treatment group. Therefore, the risk ratio for death in the control group compared to that in the intensive treatment group was 1.62 (CI: 1.22 - 2.15, p<0.001). The authors chose a difference in mean survival time of 1.5 years.

With respect to the estimate of the quality of life, 221 (78%) patients in the intensive treatment group participated in the HRQoL study, and 201 (73.4%) completed the questionnaire. 66 patients (94%) in the conventional treatment group participated in the HRQoL study, and 61 (87%) completed the forms. The results of the questionnaire indicated that prior to the treatment there was no statistically significant difference between the groups. One month after the beginning of the treatment, patients in the intensive treatment group reported lower scores compared to the control group. At 6 months, these differences were accentuated. At 12 months and beyond, both groups reported similar results.

The authors computed the utility score at 6 months in the intensive treatment group (0.7334) and in the control group (0.7896). The difference in the utility score between the intensive and the conventional treatment groups was 0.056.

Clinical conclusions
The clinical conclusion derived from the evaluation of the interventions indicated that the intensive treatment was associated with greater survival and lower utility scores compared to the conventional treatment.

Measure of benefits used in the economic analysis
Quality-adjusted life years (QALYs) were used as the measure of benefits. The utility values for health states were obtained by mapping the data from the QLQ-C30 instrument onto the 15-D health utility measure.

Direct costs
Costs were incurred over 3 years and were discounted at 5% in the base case. Direct costs were medical costs, average number of hospital days, and consultation with physicians and nurses. In the intensive treatment group, direct costs also included intensive care days and drug transfusions. Quantity and costs were reported separately and the boundary adopted for direct costs was that of the healthcare system. The estimation of costs and quantities was based on actual data and was derived from hospital records. Prices of drugs were derived from Felleskatalogen (1999). The price year was 2000.

Statistical analysis of costs
No statistical analysis of costs was reported.
Indirect Costs
Productivity losses (days lost from paid work) were considered as indirect societal costs. Costs were discounted at 5%. The authors assumed 50% productivity compensation by increased productivity in remaining employees and replacement by other workers. The average daily salary in Norway was set at about NOK 1,400. The price year was 2000.

Currency
Norwegian kroner (NOK), converted into US dollars ($). The conversion rate (year 2000) was $1 = NOK 9.25.

Sensitivity analysis
Sensitivity analyses were undertaken to investigate the uncertainty around the variability in the following parameters: the estimate of the mean survival time, the price of some drugs and other costs, the discount rate, and the utility scores.

Estimated benefits used in the economic analysis
The adoption of an intensive treatment based on HDM combined with ABSCS generated an incremental 1.2 QALYs compared to the conventional oral treatment with MP in a 3 year time period.

Cost results
The total incremental cost of HDM and ABSCS compared with MP from a societal point of view was NOK 299,000 ($32,300). Incremental direct costs amounted to NOK 226,000 ($24,400). Incremental indirect costs were NOK 73,000 ($32,300).

Synthesis of costs and benefits
Estimated costs and benefits were combined by calculating an incremental cost-utility ratio. In the base case, the estimated incremental cost-utility ratio for the intensive treatment over the conventional treatment was NOK 249,000 (NOK 299,000/1.2 or $27,000) per QALY. By changing the assumptions by 10% for cost items, the incremental cost per QALY ranged from $25,140 to $28,070. The use of a discount rate of 4% instead of 5% had no significant effect on the outcome. A wide variation of utility scores did not affect the incremental ratio. Only assuming the most favourable scenario for the intensive treatment group, the cost per QALY would decrease to $22,400. By changing the survival time (by 0.5 years either way), the incremental cost per QALY ranged from $20,200 to $40,000.

Authors' conclusions
The authors concluded that the treatment with HDM and ABSCS in newly diagnosed, symptomatic myeloma patients under the age of 60 yields a considerable gain in terms of QALYs from the societal point of view.

CRD COMMENTARY - Selection of comparators
The choice of the comparator was clearly based on the selection of the conventional treatment for patients with myeloma. You should decide whether it represents a widely used technology in your own setting.

Validity of estimate of measure of effectiveness
Very few details were reported given that the analysis of the effectiveness was carried out in a different study. However, it seems that few statistical analyses were carried out to take into account potential biases and confounding factors. This may limit the internal validity of the study because the trial was not randomised.

Validity of estimate of measure of benefit
The estimation of benefits was modelled. The instrument used to derive a measure of health benefit was the quality-
adjusted life year (QALY), which seemed to be appropriate to the objective of the study, given that the interventions aim to improve both the length and the quality of the patients' lives.

**Validity of estimate of costs**
All categories of costs relevant to the perspective adopted were included in the analysis. Future health care costs for people for whom death was averted were not included. However, as the authors stated, this omission should not have affected the result of the analysis given that there were no differences in survival between the groups. No mention was made of the technique used to estimate the survival curve.

**Other issues**
The issue of generalisability to other settings was not explicitly addressed. However, the authors made appropriate comparisons of their finding with those from other studies. In addition, sensitivity analyses were carried out on several parameters and the estimates seem quite robust. A possible limitation of the study, as the authors noted, was the lack of direct measurement of utilities and the adoption of a two-step procedure, which is a potential source of errors.

**Implications of the study**
The estimated incremental cost per QALY of the intensive treatment for young patient with multiple myeloma is below the common threshold of $50,000 used to consider a health technology cost-effective. Based on these calculations, the authors suggested that the intensive treatment is acceptable when judged relative to other cost-utility ratios of other health care interventions.

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