Cost effectiveness of aggressive care for patients with nontraumatic coma

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
Patients with nontraumatic coma were given aggressive care, which meant that there were no plans to limit life-sustaining treatments. The comparator treatment was the withholding of cardiopulmonary resuscitation (CPR) and ventilatory support by day 4 of the coma.

Type of intervention
Treatment.

Economic study type
Cost-utility analysis.

Study population
The study population comprised patients with nontraumatic coma who were enrolled in the Study to Understand Prognoses and Preferences for Outcomes and Risks of Treatments (SUPPORT). The patients had to be aged 18 years or older and meet criteria for at least one of nine diagnostic categories, one of which was nontraumatic coma. They also had to be in hospital and be alive 48 hours after entering hospital. Patients were described as being in a coma if, during the first 24 hours of their hospitalisation or while receiving care in the intensive care unit, a physician described them as being comatose, unconscious, or obtunded and they had a Glasgow coma score of less than or equal to 9 for at least 6 hours. Patients were excluded if the coma was caused by trauma, drug intoxication, hypothermia, or an operative complication. Coma caused by diabetic ketoacidosis, nonketotic hyperosmolar syndrome, thyrotoxicosis, myxedema, hepatic encephalopathy, uraemia, hyponatraemia, hypernatraemia, hypocalcaemia, or hypercalcaemia were also excluded. Patients with coma due to hypoglycaemia or hypoxemia were included.

Setting
The setting was secondary care. The economic study was carried out in the USA.

Dates to which data relate
The effectiveness and resource evidence related to 1989 to 1994. The price year was 1998.

Source of effectiveness data
The effectiveness data were derived from a single study.

Link between effectiveness and cost data
The same patients provided the effectiveness and cost data. It was unclear whether the costing was carried out prospectively or retrospectively.
Study sample
No power calculations were reported in the paper. There was no sample selection; all patients who met the inclusion criteria were included. There were 596 patients overall. They had a median age of 67 years (range: 55 - 77) and 52% were female. Information on risk factors to determine the risk status of patients was available for 549 of these patients. The less aggressive strategy was used for 40 (14%) of the 290 low-risk patients and for 81 (31%) of the 259 high-risk patients.

Study design
This was a multi-centre trial (five centres). The patients were followed up for a minimum of 6 months and a maximum of 4.6 years.

Analysis of effectiveness
The basis of the analysis was intention to treat. The primary health outcomes used were 2-month and 1-year mortality rates. On day 4 of the coma, there was no difference between high-risk patients treated aggressively and nonaggressively as regards their risk status. Among low-risk patients, those treated less aggressively had a slightly worse risk status (1.6) than those treated more aggressively (1.3), (p=0.005).

Effectiveness results
Two-month mortality was 49% for low-risk patients and 93% for high-risk patients.

For low-risk patients, 1-year mortality was 95% for those receiving less aggressive care and 58% for those receiving more aggressive care. For high-risk patients, 1-year mortality was 99% for those receiving less aggressive care and 95% for those receiving more aggressive care.

Clinical conclusions
The authors did not specifically report any clinical conclusions. However, the results showed that when patients are categorised as high-risk they have a very low life expectancy, and the provision of aggressive care hardly changes the outcome.

Modelling
Markov models were used to estimate the life-time costs and quality-adjusted life expectancy. Kaplan-Meier curves were used to estimate mortality after the follow-up had finished. A prognostic model was also used to predict 2-month mortality according to the number of risk factors. A sample of 222 patients was used to derive the prognostic model.

Measure of benefits used in the economic analysis
The measure of benefits was the quality-adjusted life-years (QALYs). QALYs were derived by combining measures of life expectancy and morbidity with measures of utility derived from interviews with the patients at 6 months' follow-up. The patients were asked to state how much time in excellent health would have the same value as living 12 months in their existing health state. If a patient were willing to exchange 12 months in their existing state for 6 months in perfect health, their utility would be described as 0.5. The health benefits were discounted at a rate of 3%.

Direct costs
A societal perspective was adopted in the analysis. The costs measured were hospital costs, physician costs, and long-term care costs after hospital discharge. The costs were estimated using actual data taken from the participating hospitals, Medicare cost-to-charge ratios, and Resource Based Relative Value Scale methodology (see Other Publications of Related Interest). The long-term care costs were taken from Tung et al. (see Other Publications of Related Interest). The quantities and the costs were not analysed separately. Hospital and physician costs after year 1 were assumed to be similar to costs incurred during the final quarter of year 1. The costs were discounted at a rate of
3%. The price year was 1998.

**Statistical analysis of costs**
The costs were not treated stochastically.

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

**Currency**
US dollars ($).

**Sensitivity analysis**
Each cost component and the annual mortality rate were varied from 50 to 200% of the baseline estimates. The utilities were varied from 0.5 to 1. The discount rate was varied from 0 to 10%. The three variables which produced the most change in outcomes (annual mortality after year 1, year 1 health care costs, and annual costs after year 1) were varied simultaneously to 67 and 150% of their baseline values.

**Estimated benefits used in the economic analysis**
The mean utility for the group who survived for at least 6 months was 0.68. The number of QALYs for each intervention and the number of QALYs gained in providing aggressive care, rather than withholding CPR and ventilatory support, were not reported.

**Cost results**
The mean hospital and physician costs of the aggressive treatment strategy were $43,198 for low-risk patients and $19,309 for high-risk patients.

The corresponding costs for withholding aggressive treatment were $9,304 (low-risk patients) and $4,489 (high-risk patients), respectively.

These costs did not include the costs after hospital discharge, which were not given for the two types of treatment.

The costs of adverse effects were dealt with in the costing.

**Synthesis of costs and benefits**
The cost per QALY gained of the more aggressive treatment was $140,000 for high-risk patients and $87,000 for low-risk patients.

In the one-way sensitivity analysis, the lowest cost per QALY gained for low-risk patients was $54,000. This was obtained by reducing the annual costs after year 1 by 50%.

In the three-way sensitivity analysis, the lowest cost per QALY gained was $57,000 for low-risk patients, while the highest was $320,000 for high-risk patients.

The authors concluded that the sensitivity analysis showed that aggressive treatment of nontraumatic coma patients produced a high cost per QALY gained compared with other commonly used medical interventions.

**Authors’ conclusions**
The aggressive treatment of nontraumatic coma patients is very ineffective and very expensive in terms of the cost per
quality-adjusted life-year (QALY) gained for patients with high-risk factors. For low-risk patients, the cost per QALY gained of aggressive treatment is still higher than many other widely accepted treatments, but the treatment is a lot more effective.

CRD COMMENTARY - Selection of comparators
The selection of the comparator was justified by it being a commonly used form of care-management in patients with nontraumatic coma. You should decide if it is a widely used intervention in your own setting.

Validity of estimate of measure of effectiveness
The source of the effectiveness data was a single study. The study was a non-randomised trial with concurrent controls. The disadvantage of this design is that the treatment may not be the only reason for the results. However, a randomised trial would not have been considered ethical. The study sample was representative of the study population as it included all patients meeting the inclusion criteria. The high-risk patients treated aggressively and nonaggressively were shown to be similar in terms of their prognosis. The low-risk patients treated aggressively had a slightly better prognosis than those treated nonaggressively. There were no other patient characteristics on which to assess the comparability of the two groups of patients. The analysis of effectiveness was handled credibly, apart from not mentioning the drawback of the lack of randomisation and potential confounding factors.

Validity of estimate of measure of benefit
The summary measure of benefit used in the economic analysis was derived through modelling, using a Markov model, which was appropriate for the study question. The measure of benefit was the QALYs, but the authors did not give the QALY results.

Validity of estimate of costs
Although the perspective adopted in the study was societal, no indirect costs were included. In addition, the analysis did not include the costs of informal care. Therefore, there is some uncertainty surrounding the validity of the cost results. The costs and the quantities were not reported separately, which limits the usefulness of the results to decision-makers in other settings. The resource use quantities were taken from a single study, while the unit costs were taken from the authors' setting. No statistical analysis of either the quantities or prices was carried out. The costs were correctly discounted using an appropriate discount rate. A sensitivity analysis was carried out on the discount rate, and the range used seems to have been reasonable. The price year was reported, which will aid any future reflation exercises.

Other issues
The authors made appropriate comparisons of their results with the findings from other studies. They also addressed the issue of the generalisability to other settings. The authors did not present detailed results for the two treatment options, but their conclusions reflect the scope of the analysis. The authors reported certain limitations of their study. First, the study focused on the decisions that were made by day 4, whereas, in reality, decisions are made throughout a patient's illness. Thus, the study might have oversimplified the complexity of real-life medical decisions. Second, it was assumed that the costs for patients without Medicare insurance were similar to those with Medicare insurance. Hence, the study underestimated the costs for the full cohort. Finally, the authors also mentioned that, if a poor prognosis is used to determine treatment, then the prognosis will affect the outcomes.

Implications of the study
The authors concluded that withholding aggressive treatment from nontraumatic coma patients with a poor prognosis may yield considerable cost-savings.

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**Other publications of related interest**


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