Impact of new treatments for neonatal pulmonary hypertension on extracorporeal membrane oxygenation use and outcome

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 studied was extracorporeal membrane oxygenation (ECMO) which is used to treat newborns with persistent pulmonary hypertension (PPHN) and its associated outcomes, both with and without the prior use of high-frequency oscillatory ventilation (HFOV) and inhaled nitric oxide (INO).

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
To be included in the study population, patients were required to weigh more than 2,000gm and to have a gestational age greater than 34 weeks. All patients were severely ill with persistent pulmonary hypertension.

Setting
The study took place at a children's hospital in the USA which was a regional referral centre and an ECMO centre.

Dates to which data relate
The effectiveness analysis relates to data collected during two periods: period 1 (1988-1990) and period 2 (1993-1995). Resource data on length of the ECMO run, duration of ventilation post-ECMO and length of hospitalisation were also collected from the same case-note source. The date of the prices used was not given.

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

Link between effectiveness and cost data
The costing was undertaken on a sub-group of the study sample, however it is not clear whether it was undertaken prospectively or retrospectively.

Study sample
The clinical records of all patients with PPHN and who met the criteria for ECMO treatment between 1988 and 1995 were retrospectively reviewed. Patients treated with ECMO (103 in total) from 1988 to 1990 (period 1) and 1993 to 1995 (period 2) were chosen for comparison since period 1 was pre-HFOV and INO and period 2 was when HFOV and INO were fully established as treatment modalities. No power calculations were performed and there is no
evidence that the patient sample was appropriate for the clinical study question. In terms of patient numbers, it was not clear how many patients were included in period 1, but it was stated that there were 96 in period 2.

**Study design**
This study was a before and after study, based on retrospective case review, which took place at a single specialist ECMO centre. Patients were followed up until hospital discharge.

**Analysis of effectiveness**
The effectiveness analysis was based on treatment completers only. The primary health outcomes used were survival and number of patients requiring ECMO. The percentage of children requiring oxygen at hospital discharge was also measured, as was length of ECMO (hours), length of ventilation post-ECMO, and length of hospitalisation for ECMO survivors (the latter measures are addressed in the cost/resource section below). It was reported that the diagnoses of the patients meeting ECMO criteria did not differ significantly between the two time periods, neither did the age of the patients at referral. Surfactant replacement therapy was used more often in period 2 but the authors do not consider this to be a confounding factor since it was used equally between patients who required ECMO and those who did not.

**Effectiveness results**
Overall ECMO survival declined from 83.6% during period 1 to 56.3% during period 2 (p<0.025) even though survival among the overall patient group with PPPHN (treated with HFOV, INO or ECMO) was not significantly different between the two periods (84% in period 1 compared with 77% in period 2). The number of patients requiring ECMO declined, from an average of 22.3 (+/- 2.3) per year during period 1 to 5.3 (+/- 2.9) during period 2 (p<0.002). The percentage of children requiring oxygen at discharge was not significantly different between the two periods. Disease severity as measured by oxygenation index and a/A ratios at the beginning of ECMO therapy were reported to be unchanged between the two time periods, as was the length of time between patient admission and ECMO cannulation.

**Clinical conclusions**
The number of patients requiring ECMO was shown to have dramatically decreased in recent years, although the reason for the higher mortality rate in the more recent period was not explainable by the authors. Side-effects were not addressed in the study although the authors commented on the necessity for long-term survival data.

**Modelling**
No modelling was undertaken.

**Measure of benefits used in the economic analysis**
No summary benefit measure was used by the authors. Therefore the benefits were assumed to be equal to the effectiveness results.

**Direct costs**
The cost data presented, relating to hospital costs only, were derived from a comparison between 8 patients treated with ECMO in 1992 with 10 patients treated with INO in 1993 who in previous years would have met ECMO criteria. No price date was given. The cost of HFOV treatment was not addressed. For the entire patient sample in the two study periods, some resource data were presented, such as length of hospitalisation, time from hospital admission to ECMO, length of ECMO, length of ventilation post-ECMO and length of hospitalisation for ECMO survivors.

**Statistical analysis of costs**
Cost results were tested for statistical significance using t-tests and chi-square analysis.
Indirect Costs
Not studied.

Currency
US dollars ($).

Sensitivity analysis
A sensitivity analysis was not performed.

Estimated benefits used in the economic analysis
No summary benefit measure was used by the authors. Therefore the benefits were assumed to be equal to the effectiveness results.

Cost results
For patients responding to INO and not requiring ECMO there was a decline in hospital costs: from $123,000 (+/- $36,096) to $65,000 (+/- $32,342); mean +/- SD, p<0.01. This sub-sample also showed a reduction in hospitalisation, from 36 (+/- 19.9) days to 21 (+/- 11.1) days. For the wider sample of patients, time from hospital admission to ECMO cannulation did not significantly increase between the periods, neither did length of ECMO, length of ventilation post-ECMO, or length of hospitalisation.

Synthesis of costs and benefits
Costs and benefits were not synthesised.

Authors' conclusions
For the reduction in survival following the use of ECMO between the two periods, no explanation was found. The authors did however note that it could, in fact, have been due to an increase in the severity of illness among patients receiving ECMO in period 2, but that the measures of disease severity used were not able to detect this. More clinical trials are necessary to establish the relative indications for the different treatment modalities, HFOV, INO and ECMO, and to investigate whether the failure of one points to prognostic significance for the others. The point is also made by the authors that declining numbers of ECMO patients may impact upon the maintenance of the skills and expertise of the ECMO team.

CRD COMMENTARY - Selection of comparators
The rationale for the selection of the comparator was justified. The study compared two time periods to investigate the impact of new treatment modalities (HFOV and INO) on the deployment and outcome of another longer established treatment modality.

Validity of estimate of measure of benefit
The study was not a randomised comparison of different treatment modalities, but a before and after investigation into the use and outcome of a health intervention between two time periods. Although the patient samples in the two time periods were investigated for confounding factors (e.g. differences in age, diagnosis and disease severity) there still remains a danger that other, unidentified factors could confound the results.

Validity of estimate of costs
Regrettably neither the components of the cost data nor the price date were stated which makes it difficult for others to
compare these results with those in their own setting. However some resource data were provided such as length of stay, and length of ventilation, which have significant resource implications.

**Other issues**
The authors were unable to explain the reduction in survival following ECMO in period 2 and it would appear that only a randomised trial can answer the issues hinted at in this paper, namely which of the differing treatment modalities for PPNH should be employed and when. Such a randomised trial should be multi-centred since results from such technically-demanding treatment modalities can differ greatly between centres with different degrees of experience.

**Implications of the study**
A randomised controlled trial is needed to validate the findings presented.

**Source of funding**
Supported in part by grant HL-46481 from the National Institute of Health and by the Bugher Physician-Scientist Training Program.

**Bibliographic details**

**PubMedID**
9373841

**Indexing Status**
Subject indexing assigned by NLM

**MeSH**
Administration, Inhalation; Costs and Cost Analysis; Extracorporeal Membrane Oxygenation /utilization; Female; High-Frequency Ventilation; Humans; Infant, Newborn; Length of Stay; Male; Nitric Oxide /administration & dosage; Persistent Fetal Circulation Syndrome /mortality /therapy; Retrospective Studies; Survival Rate; Treatment Outcome

**AccessionNumber**
21998006225

**Date bibliographic record published**
30/04/1999

**Date abstract record published**
30/04/1999