Cost effectiveness analysis of neonatal extracorporeal membrane oxygenation based on four year results from the UK Collaborative ECMO Trial

Petrou S, Edwards L

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 compared the use of neonatal extracorporeal membrane oxygenation (ECMO) with the conventional management technique for mature newborn infants with severe respiratory failure. The conventional management technique was not described in detail in the current paper.

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised mature newborn infants with a gestational age at birth of at least 35 weeks and a birth weight of at least 2,000 g, who suffered from severe respiratory failure (oxygenation index ≥ 40). No further inclusion or exclusion criteria were reported in the present paper.

Setting
The setting was secondary care (hospitals) and specialist regional centres. The economic analysis was carried out in the UK.

Dates to which data relate
Infants were recruited between January 1993 and November 1995 and each infant was followed up for 4 years. The effectiveness and resource use data were collected over the equivalent period. All of the costs were reported at the 2001 level.

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

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

Study sample
In the current paper the authors did not mention whether the sample size was determined in the planning phase to assure a certain power, or whether any power calculations were performed retrospectively. The reader is referred to the main clinical papers for information on the method used to select the sample and possible refusals to participate (UK
Collaborative ECMO Trial Group 1996 and Bennett et al. 2001, see ‘Other Publications of Related Interest’ for bibliographic details). Overall, 185 infants with severe respiratory failure were recruited between January 1993 and November 1995 for the study. Of these, 93 infants were randomly allocated to the ECMO group and 92 to the conventional management group.

Study design
The analysis was based on a pragmatic, multi-centre (55 hospitals), randomised controlled trial. The method of randomisation was not reported in the current study. Each individual was followed up for 4 years. The authors reported that five infants were lost to follow-up (2 from the ECMO group and 3 from the control group), but the reasons for withdrawals were not reported. No blinded assessment was reported.

Analysis of effectiveness
It was not reported whether the analysis was conducted on an intention to treat basis or on treatment completers only. The primary outcomes used were death and long-term disability (morbidity). Long-term disability was initially assessed at 1 year and then fully assessed at 4 years of age, using standardised neurodevelopment assessments that a single paediatrician conducted at the infant’s home. Cognitive ability, neuromotor skills, general health, behaviour, vision and the hearing of children aged 4 years were evaluated and characterised as normal, impaired, mildly disabled, moderately disabled, or severely disabled according to the degree of functional loss. Further details on the individual measures used to evaluate the outcomes were provided elsewhere (Bennett 2002, see ‘Other Publications of Related Interest’ for bibliographic details). The current study did not report whether the two groups were comparable at baseline in terms of demographics and disease factors (see UK Collaborative ECMO Trial Group 1996 and Bennett et al. 2001 in the ‘Other Publications of Related Interest’ section for relevant details).

Effectiveness results
The authors reported that the main clinical results were reported in separate papers (UK Collaborative ECMO Trial Group 1996 and Bennett et al. 2001, see ‘Other Publications of Related Interest’).

At 4 years of age, the ECMO group demonstrated both an increased number of survivors (62 versus 38) and an increased number of survivors who were free of disability (30 versus 13), compared with the conventional management group. However, the ECMO group had a higher number of survivors with severe disability (3 versus 0 in the conventional group).

Overall, the authors reported that the ECMO technique resulted in 34 (37%) cases of death and severe disability versus 54 (59%) cases in the conventional management group (relative risk 0.64, 95% confidence interval, CI: 0.47 - 0.86; p=0.004).

Clinical conclusions
The authors concluded that the ECMO technique is more clinically effective than conventional management strategies for infants with severe respiratory failure.

Measure of benefits used in the economic analysis
The measures of benefit used were the life-years gained and the disability-free life-years gained. The authors reported that to avoid subjective valuations for each state of impairment, they evaluated each infant whose overall disability during the 4-year period was not classified as impaired or disabled in terms of disability-free life-years. The health benefits incurred after the first year were discounted at an annual rate of 1.5%.

Direct costs
The health service costs included in the economic analysis were for:
road transportation with ambulance;

the initial hospital stay (including costs of days on ECMO, on >90% oxygen, on ventilator and on supplemental oxygen at any different concentration);

an infant death;

an inpatient hospital readmission;

an outpatient hospital visit;

a visit to a general practitioner;

a health visitor visit;

a visit to other community carers (including paediatrician, community nurse, physiotherapist, outpatient therapist, speech therapist, psychologist, counsellor, ophthalmologist, optometrist, orthoptist and audiologist); and

drugs.

The quantities of resources used and the costs were analysed separately. The quantities were derived from the single study, using patients' records and interviews or observational work. The costs were estimated using actual data and data from published sources. All the costs incurred after the first year were discounted at an annual rate of 6% and were reported for the fiscal year 2001.

**Statistical analysis of costs**

All of the results were reported using descriptive statistics (mean values and standard deviations) and, when possible, 95% CIs were reported for mean differences in the costs. Differences in the costs between the two groups were tested using Student's t-test, where a two-tailed p-value of 0.05 or less was considered statistically significant. In addition, a non-parametric bootstrap technique was used to derive 95% CIs for the mean cost-differences between the two groups.

**Indirect Costs**

The indirect costs were not included in the analysis.

**Currency**

UK pounds sterling (£).

**Sensitivity analysis**

Various multi-way sensitivity analyses were carried out to test the robustness of the resultant cost-effectiveness ratios and variability in the data. The daily costs were altered by +/- 20%, while the use of community services was increased by 10, 20 and 30%. The discount rates applied to the costs and effects were also varied. Cost-effectiveness acceptability curves were built assuming an NHS willingness-to-pay threshold of 30,000 for an additional life-year gained or additional disability-free life-year gained.

**Estimated benefits used in the economic analysis**

The estimated benefits used in the economic analysis were not reported separately for each treatment group.

**Cost results**

The mean (standard deviation) total costs per infant were 26,053 (21,058) in the ECMO group and 8,686 (15,489) in the conventional management group.
The mean difference in costs was 17,367, which was statistically significant, \((p<0.0001)\). The bootstrap mean difference in costs was 17,321 (95% CI: 12,072 - 22,224).

**Synthesis of costs and benefits**
The authors performed an incremental analysis. The incremental cost per additional life-year gained was 16,707, while the incremental cost per additional disability-free life-year gained was 24,775.

Assuming an NHS willingness-to-pay threshold of 30,000 for an additional life-year gained or an additional disability-free life-year, the probability that neonatal ECMO is cost-effective at 4 years was 0.94 and 0.69, respectively.

The sensitivity analyses demonstrated that the results remained robust after the input parameters were varied.

**Authors’ conclusions**
The current study provided rigorous evidence of the cost-effectiveness of neonatal extracorporeal membrane oxygenation (ECMO) at 4 years for mature infants with severe but potentially reversible respiratory failure.

**CRD COMMENTARY - Selection of comparators**
The choice of the comparators used was explicitly justified. The baseline comparator, the conventional management technique, appears to have represented common practice in the authors’ setting. You should decide if this represents a widely used technology in your own setting.

**Validity of estimate of measure of effectiveness**
The analysis was based on a randomised controlled trial, which was appropriate given the study question. However, it was not possible to comment on the internal validity of the effectiveness results since the authors referred to a separate clinical paper for details of the clinical study. For example, details on a power calculation to determine sample size, methods of randomisation and blinding were not reported in the present study. In addition, the baseline characteristics of the two groups and a statistical analysis to compare the groups at baseline were not reported. Therefore, it was unclear whether the study sample was representative of the study population.

**Validity of estimate of measure of benefit**
The measures of benefit used were the life-years gained and the disability-free life-years gained. Disability was fully and appropriately evaluated by professionals. The authors acknowledged that a measure of quality-adjusted life-years (QALYs), which incorporates societal preferences for each possible health outcome, would have been more appropriate for comparative purposes.

**Validity of estimate of costs**
The cost analysis was performed from the perspective of the health service (NHS). The authors provided a thorough and detailed examination of the costs faced by the NHS. The costs and the quantities were reported separately, thus enhancing the reproducibility of the study in other settings. The resource quantities were derived directly from the study, while most of the unit costs were derived from published sources. An appropriate statistical analysis of the costs was undertaken. In addition, the authors carried out several sensitivity analyses, which improve both the internal validity and the generalisability of the study by demonstrating the robustness of the results to changes in the estimated variable values. As the time horizon of the economic evaluation was 4 years, discounting was appropriately conducted. In addition, the price year was reported, thus aiding future reflation exercises.

**Other issues**
The authors did not compare their findings with those from other studies, so it is not known how far their results agree with other published results. However, they directly addressed the issue of generalisability of the results to other settings.
through the sensitivity analysis (see also the limitations highlighted below). The authors do not appear to have presented their results selectively. The study enrolled mature infants with severe respiratory failure and this was reflected in the authors’ conclusions.

The authors reported a number of limitations to their study. First, differences in the costs and outcomes between the two groups might have been overestimated in case they referred to greater experience and infrastructure in the ECMO special centres, rather than to the plain effect of ECMO. Second, according to the perspective adopted, costs related to the procedure but not incurred by the health service (e.g. societal costs such as costs borne by the parents or productivity losses) were not included, thus the incremental cost of each outcome might have been underestimated in the ECMO group. Third, the measure of benefit used was not a single metric accounting for societal preferences (e.g. QALYs). Fourth, the authors also referred to the fact that the short time horizon of the economic evaluation prohibited the evaluation of the long-term cost-effectiveness of the ECMO technique. Finally, the authors reported that their estimates of the NHS willingness-to-pay thresholds for particular health gains were random and that they represented the current threshold value per QALY in the UK.

**Implications of the study**
The authors draw the attention of decision-makers to decide whether the results of the study are applicable to their own settings. If they are, they should first evaluate the economic impacts of the implementation of such a technique due to its high costs. In addition, the authors referred to additional research they plan to undertake. More specifically, the goal of incorporating measurements of health-related quality of life of the survivors in order to estimate an incremental cost-utility ratio for ECMO, and to conduct a lifetime economic evaluation of the procedure.

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**Other publications of related interest**


**Indexing Status**
Subject indexing assigned by NLM

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