Efficacy and economic assessment of conventional ventilatory support versus extracorporeal membrane oxygenation for severe adult respiratory failure (CESAR): a multicentre randomised controlled trial
Peek GJ, Mugford M, Tiruvoipati R, Wilson A, Allen E, Thalanany MM, Hibbert CL, Truesdale A, Clemens F, Cooper N, Firmin RK, Elbourne D, the CESAR trial collaboration

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.

CRD summary
This study investigated the costs and clinical outcomes of extracorporeal membrane oxygenation (ECMO), compared with conventional ventilation support, for adults with severe respiratory failure. The authors concluded that ECMO was clinically superior and cost-effective compared with conventional treatment. The effectiveness results for ECMO appear to be valid, but the lack of detail on the methods makes it difficult to ascertain, from this paper alone, whether or not the authors’ conclusions are reasonable.

Type of economic evaluation
Cost-effectiveness analysis, cost-utility analysis

Study objective
The aim was to assess the costs and health effects of extracorporeal membrane oxygenation (ECMO), compared with those of conventional ventilation support, for severe respiratory failure. The population comprised adults with a mean age of 40 years, 52% of whom were male, and approximately 60% had a primary diagnosis of pneumonia.

Interventions
ECMO was compared against the best practice conventional support for patients with severe, but potentially reversible respiratory failure. The best practice varied, but low-volume low-pressure ventilation was encouraged.

Location/setting
UK/in-patient.

Methods
Analytical approach:
The economic evaluation was undertaken alongside a single, multi-centre, prospective, randomised clinical trial, called the Conventional ventilation or ECMO for Severe Adult Respiratory failure (CESAR) trial (Peek, et al. 2006, see ‘Other Publications of Related Interest’ below for bibliographic details). Modelling was also undertaken to extend the time horizon. The two time horizons were six months and lifetime. The authors reported that the perspectives were those of the UK National Health Service (NHS) and of patients and carers.

Effectiveness data:
The primary clinical outcomes included death or severe disability at six months. Severe disability was defined as confinement to bed and inability to wash or dress alone. Secondary outcomes included duration of ventilation, use of high frequency oscillation, jet ventilation, use of nitric oxide, prone positioning, use of steroids, duration of intensive care stay, hospital stay, and health status. The clinical data were derived from the CESAR trial (Peek, et al. 2006). The sample size was 180 patients, and the trial was adequately powered to detect significant differences in mortality. An intention-to-treat analysis was undertaken without adjustments for any potential confounders.

Monetary benefit and utility valuations:
The health states of the trial participants were measured using the European Quality of life (EQ-5D) questionnaire and valued using UK population tariffs.
Measure of benefit:
The measure of benefit was quality-adjusted life-years (QALYs) and they were discounted at 3.5% per annum.

Cost data:
The resource data were for hospital care, patient transport to ECMO centre, and patient use of health service resources (Thalanany, et al. 2008, see ‘Other Publications of Related Interest’ below for bibliographic details). Case-mix-adjusted average costs per day in critical care were used to value hospital care and these excluded hospital overheads. Published sources were used for resource valuation. Patient health service use data were collected by postal surveys at six months. The costs were discounted at 3.5% per annum and reported in 2005 UK pounds sterling (£) and US dollars ($). Pounds were converted to dollars using purchasing power parities from the Organisation for Economic Cooperation and Development.

Analysis of uncertainty:
Sensitivity analysis was used to test variations in the key cost estimates. A complete case analysis was also undertaken and the base-case analyses were compared with a scenario in which missing costs were filled using Rubin's multiple imputation methods. Non-parametric bootstrapping methods were used to assess the uncertainty in the incremental cost-utility ratios.

Afternote:
: fuller details for the economics methods used in the CESAR trial can be found in a Health Technology Assessment report published in 2010 after this abstract was written (Peek et al 2010, see 'Other publications of related interest' below for bibliographic details.

Results
The mean discounted costs were £73,979 for the ECMO group and £33,435 for conventional treatment at six months. The discounted six-month incremental cost for ECMO versus conventional treatment was £40,544 (95% CI 24,799 to 56,288). The discounted lifetime incremental costs were £48,533 and QALYs were 3.66, for ECMO versus conventional treatment.

The incremental cost-utility ratio was £19,252 (95% CI 7,622 to 59,200). The incremental cost per additional surviving patient without severe disability was £250,162. The costs were sensitive to the costing methods used for critical care units.

Authors' conclusions
The authors concluded that referral for ECMO was more effective than conventional management, of patients with severe respiratory failure, and the lifetime cost-utility of around £19,000 was likely to be cost-effective in the UK and similar settings.

CRD commentary
Interventions:
The intervention and control groups were fully described and the conventional management group reflected the usual clinical practice in the participating centres in the UK. ECMO may be an appropriate comparator in other settings, but circumstances, such as the need to transport a patient by air, might be different and should be considered.

Effectiveness/benefits:
The effectiveness data were based on a multi-centre randomised controlled trial, which was powered to detect meaningful differences in the primary outcomes. Another publication, by the authors (Peek, et al. 2006), contained further information on the success of randomisation, crossover effects, and quality of the clinical findings. The utility values were appropriately measured using the UK-recommended EQ-5D questionnaire.

Costs:
The costing methods were not reported in detail in this paper, but the details were presented in another publication (Thalanany, et al. 2008), which should be consulted to assess these methods and whether they reflected the study perspective. The method used to extrapolate the costs, beyond the duration of the trial, to a lifetime horizon, was not
reported. This lack of details on the methods makes it difficult to decide whether they were appropriate or not.

**Analysis and results:**
Patient exclusions and withdrawals from the analysis were presented in a flow diagram. The socio-demographic and clinical data were comprehensively reported, as were all clinical outcomes for the two groups. The base-case incremental cost-effectiveness ratios were clearly reported, but the sensitivity analysis results appear to have been reported selectively and the rationale for this selection was not explained. The authors presented a thorough discussion on the issues in their study and they acknowledged the limitations in generalising the results to other countries, where the conditions might differ.

**Concluding remarks:**
The clinical effectiveness results were comprehensive and valid, but there were no details on how these results were extrapolated to a lifetime and there was a lack of costing detail, in this paper. These issues make it difficult to assess whether or not the authors’ conclusions reflected the economic analyses undertaken.

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