Cost-effectiveness of exogenous surfactant therapy in pediatric patients with acute hypoxemic respiratory failure

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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 study assessed the use of exogenous surfactant in the treatment of paediatric acute hypoxaemic respiratory failure (AHRF).

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
The hypothetical study population comprised paediatric-aged patients with AHRF who required mechanical ventilation in the paediatric intensive care unit (PICU).

Setting
The authors stated that the study was undertaken in a tertiary care setting. The economic study was carried out in the USA.

Dates to which data relate
The effectiveness and resource data related to 1999. The year from which the prices were taken was not reported, but the authors stated that the costs were presented in 2001 US dollars.

Source of effectiveness data
The authors stated that a review of the literature was conducted, but that only one prospective randomised controlled study (RCT) was found. Consequently, the evidence of effectiveness was derived from a single study.

Link between effectiveness and cost data
The resource use data were derived from the same patient sample as that used in the effectiveness analysis. The resource use data were collected alongside the effectiveness study.

Study sample
The study sample consisted of patients with AHRF. AHRF was defined as diffuse bilateral pulmonary infiltrates, the need for ventilation support, and an oxygenation index of at least 7. Patients were excluded if they had pre-existing chronic lung disease or uncorrected congenital heart disease. The study recruited 42 patients. Further details about the study sample can be found in the parent study (Willson et al. 1999.).
Study design
The study was an RCT in which the patients were treated in one of eight tertiary medical centres. Further details about the study design can be found in the parent study (Willson et al. 1999).

Analysis of effectiveness
The primary outcome taken from the study was days in the PICU. The method of analysis used in the clinical study and the baseline characteristics of the study sample can be found in the parent study (Willson et al. 1999).

Effectiveness results
The authors used the results of the clinical study to calculate that the probability of remaining alive in the PICU for any day was 0.9201 in the surfactant group and 0.9470 in the standard group.

The probability of death for any day in the PICU was assumed to be 0.0082 for both groups.

The probability of moving from alive in PICU to alive out of PICU was assumed to be the remaining probability for each treatment group.

Clinical conclusions
The use of a surfactant could reduce the number of days in the PICU for children with AHRF.

Modelling
A Markov model was used to extrapolate the results from the clinical trial to the maximum follow-up reported in the clinical trial (44 days). The model consisted of four health states, which were alive in the PICU, alive out of the PICU, alive discharged and dead. The model had a cycle length of 1 day and analysed a hypothetical cohort of 1,000 patients.

Measure of benefits used in the economic analysis
Percentage survival was the measure of health benefit used in the economic analysis.

Direct costs
The study included the direct costs to the hospital for acquisition of the surfactant, length of stay in the PICU, and length of stay outside of the PICU. The price of the surfactant came from an unspecified source. The resource use quantities were not reported separately from the costs. The cost of inpatient days in the PICU and outside of the PICU were derived from reimbursement rates for the diagnosis-related groups (DRG) for simple pneumonia and respiratory diagnosis with ventilator support for greater than 96 hours. A Markov model was used to extrapolate the costs to the longest follow-up reported in the clinical study (44 days). Discounting was not relevant given the short time horizon. The study reported the average costs in 2001 dollars.

Statistical analysis of costs
The authors did not have access to sampled data.

Indirect Costs
The indirect costs were not included in the analysis, which was appropriate given that the study was conducted from a hospital perspective.

Currency
Sensitivity analysis
A one-way sensitivity analysis was used to explore the generalisability of the results, based on the patient’s weight (10 to 70 kg), and to explore variability in the data on the cost of inpatient days. The cost per inpatient day in the PICU was varied between $2,000 and $12,000, while the cost per inpatient day outside the PICU was varied between $1,000 and $8,000. The authors did not specify the sources of the ranges tested.

Estimated benefits used in the economic analysis
The results of the model indicated that 90.3% of patients in the surfactant group survived to 44 days, compared with 85.1% of patients in the standard group. The side effects of treatment were not considered in the analysis.

Cost results
The cost per patient was $62,922 in the surfactant group compared with $74,006 in the standard group.

Treatment with surfactant ceased to be cost-saving if the cost per hospital day outside of the PICU rose from $1,540 in the base-case analysis to greater than $7,498.

The results were not sensitive to variations in the cost of inpatient days in the PICU.

Surfactant therapy was not cost-saving in children weighing 60 or 70 kg.

Synthesis of costs and benefits
Surfactant was the dominant treatment option in the base-case analysis that included a hypothetical cohort of patients weighing 10 kg.

For the sensitivity analyses where surfactant was not the dominant treatment option (i.e. not associated with the highest survival and least cost), the costs and benefits were synthesised to calculate the cost per life saved. The cost per life saved was estimated to be $79,805 for patients weighing 70 kg.

Authors’ conclusions
The use of surfactant in paediatric patients with acute hypoxaemic respiratory failure (AHRF) can result in cost-savings from the perspective of a hospital.

CRD COMMENTARY - Selection of comparators
The comparator was chosen to represent current practice. The authors discussed other therapies used in the PICU in addition to standard care for AHRF, including extracorporeal membranous oxygenation and inhaled nitric oxide, but they did not compare these alternatives with surfactant in the economic analysis. Thus, the model did not compare all the relevant alternatives. You should consider whether standard care in the study setting is representative of current practice in your own setting.

Validity of estimate of measure of effectiveness
A single study provided the effectiveness data. The authors acknowledged that the small sample size represents a limitation of their study, but stated that no other prospective RCTs were available in the relevant patient population. Based on the information available in this paper, the study design and study sample appear to have been appropriate for the study question. The effectiveness results were treated as point estimates, so the uncertainty around the estimate of effectiveness was not reflected in the study results. The Markov model was used to extrapolate the effectiveness evidence to 44 days using a constant transition probability. The study sample is likely to have been too small to estimate
whether there was evidence of time dependency in the probability of remaining alive in the PICU.

**Validity of estimate of measure of benefit**
The estimation of benefits was modelled using a Markov state-transition model to estimate the percentage survival in each patient group over a time horizon of 44 days. The authors assumed that the probability of death in the PICU was the same for both groups, as the clinical study had shown no statistically significant difference in mortality. However, in the model, the risk of death was lower once patients left the alive in PICU state. Thus, the lower probability for remaining in the PICU for the surfactant group translates to a survival benefit. This could potentially be inconsistent with the assumption of no difference in mortality based on the results of the clinical trial.

**Validity of estimate of costs**
The study did not include the costs of adverse events or knock-on costs. Apart from these omissions, the study included all relevant costs for the hospital perspective adopted. Since the authors did not mention any potential differences in adverse events between the study groups, the effect of the omission of adverse event costs was unclear. A sensitivity analysis of the quantities was not conducted, which means uncertainty in the estimates of resource use was not reflected in the study results. The unit costs were based on reimbursement rates for DRGs in the study setting. The authors acknowledged that this may limit the generalisability of the study results to hospitals that are reimbursed on a per diem basis, and to hospitals outside of the USA. Variability in the costs of inpatient days was explored in one-way sensitivity analyses. Discounting was not relevant given the short time horizon of the model. The authors provided the price year for the analysis.

**Other issues**
The authors made appropriate comparisons of their results with findings from studies of neonatal patients with AHRF, in whom surfactant is used routinely. The issue of generalisability to other settings was addressed thoroughly. The authors did not present their results selectively, but they failed to propagate uncertainty in the model parameters through the model results. The authors' conclusions reflected the scope of the analysis. The authors acknowledged the limitations of their analysis.

**Implications of the study**
The authors recommended that future economic evaluations should incorporate results from further RCTs in this patient population.

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