Outcomes and cost-effectiveness of ventilator support and aggressive care for patients with acute respiratory failure due to pneumonia or acute respiratory distress syndrome


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 provision and withholding of mechanical ventilation and intensive care for patients with acute respiratory failure due to pneumonia or acute respiratory distress syndrome (ARDS).

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised patients with acute respiratory failure severe enough to require ventilator support. The study sample comprised patients with acute respiratory failure enrolled in the Study to Understand Prognoses and Preferences for Outcomes and Risks of Treatments (SUPPORT). Inpatients were enrolled from June 1989 until January 1994 at five geographically diverse academic medical centres. Patients eligible for SUPPORT were aged 18 or older and met criteria set for a minimum of 1 of 9 diagnostic categories. Patients were considered to have acute respiratory failure if they required treatment in the intensive care unit, had a diagnosis of pneumonia or acute respiratory distress syndrome (ARDS), and also had an Acute Physiology Score from APACHE II of 10 or more.

Setting
The setting was secondary care in the USA.

Dates to which data relate
The effectiveness and resource data were gathered between June 1989 and January 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 cost data were prospectively collected alongside the effectiveness data and from the same patient sample.

Study sample
The authors did not report the use of power calculations to determine the sample size. A total of 4,301 patients were enrolled into the SUPPORT study, upon which this study was based, and, of these, 2,500 patients had acute respiratory failure. The study sample used for this study consisted of the 1,005 patients who either received ventilator support, or
who had ventilator support withheld when imminent death was likely without such treatment. Of these, 963 had received ventilator support, whilst 42 patients had ventilator support withheld. There were differences between the intervention and control groups at baseline.

The patients who received ventilator support were divided into three-risk categories.

High-risk patients were defined as those with a 50% or less probability of surviving at least 2 months. Medium-risk patients were defined as patients with a 51%-70% probability of surviving more than 2 months, whilst low-risk were defined as those patients with more than a 70% probability of surviving at least 2 months. High-risk patients were 64 (+/- 17) years old, had an Acute Physiology score of 81 (+/- 23) and had 1.5 (+/- 1.2) co-morbid illnesses. Medium-risk patients were 66 (+/- 15) years old, had an Acute Physiology Score of 65 (+/- 15), and had 1.6 (+/- 1.3) co-morbid illnesses. Low-risk patients were 50 (+/- 18) years old, and had an Acute Physiology score of 55 (+/- 16), and had 1.3 (+/- 1.2) co-morbid illnesses.

Of the patients from whom ventilation support was withheld the mean age was 73 (+/- 14) years, the mean number of co-morbid illnesses was 1.6 (+/- 1.3), and the mean APACHE III Acute Physiology Score on study day 1 was 60 (+/- 20).

The authors did not report the risk category of these patients, although they stated that this was calculated for all members of the study sample.

**Study design**

The study was a prospective cohort study carried out in 5 geographically diverse academic medical centres. The duration of follow-up was 6 months. At 6 months, 498 (52%) of the ventilator support group had died. Dependency data was available for 359/465 (77%) of the ventilator support group who survived. The authors did not report the reasons for loss to follow-up in this group. In the group with no ventilator support, 38 (90%) died within 1 month.

**Analysis of effectiveness**

The analysis was based on treatment completers only. Patients who were discharged or died within 48 hours of study entry were excluded. The primary outcome measure was the survival rate of patients at 6 months.

The secondary outcome measures were:

- the dependence of patients in daily living;
- the functional status of patients measured using a modified version of the Katz Activities of Daily Living Scale;
- patients' quality of life measured on the following scale: excellent, very good, good, fair, or poor.

The two groups were comparable in terms of gender. There were differences in age, number of co-morbid illnesses and APACHE II Scores. The authors did not report whether these were statistically significant or whether the analysis controlled for any differences at baseline.

**Effectiveness results**

Of the 963 patients who received ventilator support 48% survived for at least 6 months, and the median survival time was 137 days. In contrast, of the patients from whom ventilation support was withdrawn the median survival was 3 days and 90% had died within 1 month.

At the 6-month follow-up the functional status and quality of life of patients who had received ventilation support was good. The median dependency in activities of daily living was 1, and overall 72% reported that their quality of life at 6 months was good, very good, or excellent (excellent = 14%, very good = 25%, good = 32%, fair = 23%, poor = 6%).
Clinical conclusions
The study revealed that the provision of ventilation support and intensive care in the treatment of patients with acute respiratory failure caused by pneumonia or ARDS is more effective than the withholding of ventilation and intensive care.

Modelling
The study used a Markov state-transition model to estimate the expected lifetime costs and quality-adjusted life expectancy of the two treatment strategies: providing ventilator support and intensive care and withholding ventilator support and intensive care.

The study also used a prognostic model to estimate the probability of surviving at least 2 months from the time of diagnosis of acute respiratory failure.

Measure of benefits used in the economic analysis
The measure of health benefit used in the economic analysis was quality-adjusted life-years (QALYs). This was estimated as mean utility multiplied by predicted life expectancy. Patients’ utility values were estimated using time-trade-off questions.

Direct costs
The study did not report costs and quantities separately, and included only direct medical costs. Total hospital charges were collected from the participating hospitals' billing systems. Hospital costs were estimated through adjusting charges using the Medicare cost-to-care ratios for the Uniform Bill 1982 (UB82) cost centres at each participating hospital. The authors estimated the cost of the portion of the index hospitalisation incurred after the initiation or withholding of ventilation support based on the percentage of the total hospital stay that occurred after ventilator support was begun or withheld. The authors linked Medicare financial data with SUPPORT data to provide estimates of hospitalisation costs after the index hospitalisation and to estimate physician costs during and after the hospitalisation. The authors assumed that the costs of patients without Medicare cover were similar to those of Medicare patients. Physician costs were estimated using the Resource-Based Relative Value Scale methodology. The annual costs after year 1 were estimated on the basis of costs incurred during the final quarter of year 1, and it was assumed that future costs would be the same in all three risk groups. The price year was 1998, and discounting was carried out at a rate of 3%.

Statistical analysis of costs
No statistical analysis of differences in costs was included in the study, although standard deviations for cost estimates were reported.

Indirect Costs
Although the authors reported that costs were estimated from the societal perspective, indirect costs were not included.

Currency
US dollars ($). No conversion rate was reported.

Sensitivity analysis
The authors used one-way, two-way and three-way sensitivity analysis. For the one-way sensitivity analyses the authors varied each cost estimate and the estimate for annual mortality after year 1 from 50% to 200% of baseline estimates. Additionally the authors also varied the utilities from the 10th to the 90th percentile (0.5 to 1.0) and the discount rate from 0% to 10%. In order to enable an estimate to be made for the group of patients at a very high risk of death, the authors calculated a cost-effectiveness ratio for patients with a 90% 1-year mortality. The two and three-way sensitivity analyses were used to test the variables that were most sensitive in the one-way sensitivity analysis. These included the
annual mortality after year 1, year 1 health care costs and annual health care costs after year 1. The authors varied the estimates across the range of 67% to 150% of baseline values to bias the results in the opposite direction of the findings of the baseline analyses.

For the low-risk patients the authors increased the estimates to 150% of baseline values to bias the analysis towards finding a higher cost per QALY. For the high-risk patients the authors decreased the estimates to 67% of baseline values to bias the findings towards finding a lower cost per QALY. The three-way sensitivity analysis represented modified best-case and worst-case analyses, in which the authors simultaneously increased or decreased all three variables in order to bias the results against the findings of the baseline analyses. Furthermore the authors also analysed the stability of the cost-effectiveness estimates through varying the baseline estimates for the costs of the index hospitalisation across the lower and upper limits of the 95% confidence interval.

**Estimated benefits used in the economic analysis**

The mean one-year survival rate for each of the three-risk categories was as follows:

- low-risk patients (greater than 70% estimated survival) = 0.62;
- medium-risk patients (51% to 70% estimated survival) = 0.39;
- high-risk patients (50% or less estimated survival rate) = 0.21.

The mean utility (quality of life weight) of all three patient risk categories was estimated at 0.88 (+/- 0.12), with a median utility of 0.92.

**Cost results**

The cost results for each of the three risk categories in the ventilator support group are shown below.

- Hospital costs for index hospitalisation (after initiation of medical treatment): low-risk patients $59,096 (+/- $64,336); medium-risk patients $70,130 (+/- $85,300); high-risk patients $59,310 (+/- $54,590).

- Physician costs for index hospitalisation: low-risk patients $5,034 (+/- $6,705); medium-risk patients $6,162 (+/- $5,264); high-risk patients $6,474 (+/- $7,426).

- Hospitalisation costs and physician costs from discharge through year 1: low-risk patients $22,037 (+/- $44,847); medium-risk patients $18,772 (+/- $42,253); high-risk patients $11,994 (+/- $34,475).

- Annual costs after year 1: low-risk patients $18,265 (+/- $48,078); medium-risk patients $13,053 (+/- $26,519); high-risk patients $28,102 (+/- $86,998).

The cost of the index admission for the group with no ventilator support was $10,913 (+/- $12,656).

**Synthesis of costs and benefits**

The study reported incremental cost-effectiveness ratios (ICERs) calculated as the cost ($) per QALY of providing, rather than withholding, ventilator support and intensive care for each of the three patient risk categories.

The cost per QALY in low-risk patients was $29,000, increasing to $44,000 in medium-risk patients and rising to $110,000 per QALY in high-risk patients.

Within the one-way sensitivity analysis the cost per QALY for the low-risk patients was between $19,000 and $52,000. For the medium-risk patients the cost per QALY was between $29,000 and $78,000. For the high-risk the cost per QALY was between $67,000 and $200,000.

Within the two-way sensitivity analysis that varied year 1 health care costs, annual health care costs after year 1, and
annual mortality after year 1, values did not exceed $50,000 per QALY for low-risk patients or fall below $50,000 per QALY for high-risk patients. The cost-effectiveness ratios ranged from $38,000 to $44,000 for low-risk patients and from $70,000 to $84,000 for high-risk patients.

Within the three-way sensitivity analysis the cost-effectiveness ratio was below $50,000 for low-risk patients and above $50,000 for high-risk patients. When the authors simultaneously increased year 1 health care costs, annual health care costs after 1 year and annual mortality after year 1 to 150% of baseline estimates, the cost per QALY was $47,000 for low-risk patients. For high-risk patients when the authors simultaneously decreased these variables to 67% of baseline estimates, the cost per QALY was $62,000.

The authors also conducted a sensitivity analysis assessing the 95% confidence intervals for the index hospitalisation costs. The ranges for the cost-effectiveness ratios were $28,000 to $30,000 per QALY for low-risk patients, $41,000 to $47,000 per QALY for medium-risk patients and $100,000 to $120,000 per QALY for high-risk patients.

Authors' conclusions
The authors concluded that the provision of ventilator support and intensive care for patients with acute respiratory failure due to pneumonia or ARDS is relatively cost-effective for patients with relatively good short-term prognoses (expected 2 month survival greater than 50%). However, for patients with a less than 50% chance of surviving at least 2 months, ventilation support and intensive care cost in excess of $100,000 per QALY, which does not compare favourably with other commonly used medical interventions.

CRD COMMENTARY - Selection of comparators
The authors reported that ventilation and intensive care is expensive, many patients die and the relative cost-effectiveness of the approach is unknown. The authors did not report whether withholding ventilator support represents current practice for a large proportion of people who may be eligible. You, as a user of this database, should decide if the comparator represents current practice in your own setting.

Validity of estimate of measure of effectiveness
The analysis was based on a large prospective cohort study. Although this design can introduce bias into the data by lack of control on the allocation of patients to the intervention and control groups, it is not clear that randomisation would have been acceptable to health care professionals or ethical committees. There were some differences in patient characteristics at baseline. The authors did not report the risk category of the group who did not receive ventilator support. The authors did not report whether the intervention and control were statistically comparable at baseline.

It was not reported whether the differences in patient characteristics were sufficient to statistically increase the risk of death in the group who had no ventilator support. This is particularly important if these factors influenced the allocation of patients to ventilator support or no ventilator support. If they did, then the analysis could be biased. It appears that the study sample was representative of the study population. The authors used sensitivity analyses rather than statistical techniques to explore the impact of potential biases and confounding factors. The sensitivity analysis used was not sufficient to control for the potential biases in patient allocation.

Validity of estimate of measure of benefit
The estimation of benefits was obtained directly from the effectiveness analysis and the choice of estimate was justified and appeared appropriate.

Validity of estimate of costs
Although the authors reported that costs were estimated from a societal perspective, indirect costs were not included. Furthermore the authors stated that their estimation of health care costs after the index hospitalisation was based on Medicare data and assumed that costs for patients without Medicare insurance were similar. However, the authors also stated that previous analyses of SUPPORT data have demonstrated that older age is associated with lower healthcare
costs, and that consequently they may have underestimated the mean costs for the full cohort whose median age was 63 years. The authors did not report costs and quantities separately and no statistical analysis of costs was performed. The results from the study were extrapolated using Kaplan Meier techniques in order to estimate survival probability three years after treatment and beyond. The authors conducted an extensive sensitivity analysis of prices and the date of the prices was reported, although the currency conversion rate was not reported. Prices were discounted at a rate of 3%, and this was varied over an appropriate range of 0% to 10% during the sensitivity analyses.

Other issues
The authors made appropriate comparisons of their findings with those from other studies. They stated that, whilst other studies reported cost-effectiveness as the cost per survivor or per year of survival, their study provided estimates of cost per QALY and thus conformed to the recommendations of the Panel on Cost Effectiveness in Health and Medicine. In addressing the issue of the generalisability of the results to other settings the authors stated that the estimates of survival, quality of life and initial hospital costs were based on data from five geographically diverse medical centres. Consequently the authors noted that the clinical outcomes and health care costs for patients treated at other centres may differ.

Implications of the study
The authors concluded that the provision of ventilator support and intensive care for patients with acute respiratory failure due to pneumonia or ARDS is relatively cost-effective for patients with a relatively good short-term prognosis (expected 2 month survival greater than 50%). However for patients with a less than 50% chance of surviving at least 2 months ventilation support and intensive care cost in excess of $100,000 per QALY, a figure, which does not compare favourably to other well established medical interventions. The authors advise that whilst the data does not provide a suitable basis for decision making in individual patients, increased understanding of the relative costs and benefits of life-extending interventions may be useful in informing discussions concerning approaches to optimising the allocation of limited health care resources.

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