Noninvasive positive pressure ventilation in the setting of severe, acute exacerbations of chronic obstructive pulmonary disease: more effective and less expensive

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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
Standard therapy (oxygen, bronchodilators, steroids, and antibiotics) plus non-invasive positive pressure ventilation (NPPV) versus standard therapy in cases of acute exacerbations of chronic obstructive pulmonary disease. NPPV is usually provided for a minimum of 8 hours on the first day and reduced gradually during the next few days.

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
The study population was patients with acute, severe exacerbations of chronic obstructive pulmonary disease (COPD), as identified by increased shortness of breath with or without cough and wheeze, and accompanied by significant respiratory acidosis. The population did not include those with excessive respiratory secretions, facial deformity that would prevent adequate fitting of the mask, and those needing immediate intubation and mechanical ventilation owing to cardiac or respiratory arrest, haemodynamic instability, or decreased level of consciousness.

Setting
The setting was a tertiary care teaching hospital in Canada. The economic study was carried out using a theoretical model and applying costing from a tertiary care teaching hospital in Canada.

Dates to which data relate
Effectiveness data were taken from studies published between 1993 and 1998. Resource data were taken from studies published between 1986 and 1996. The price year was 1996.

Source of effectiveness data
Effectiveness data were based on a review or synthesis of previously published studies.

Modelling
A decision tree based model was used to estimate the costs of the two treatment alternatives. The decision tree represented 14 possible alternative patient treatment pathways for each of the two interventions.

Outcomes assessed in the review
The review of the literature for effectiveness data looked for outcomes in terms of mortality (hospital survival) and the
need for conventional mechanical ventilation (intubation).

**Study designs and other criteria for inclusion in the review**
The effectiveness data were taken from a previous meta-analysis of randomised controlled trials (RCTs) (Keenan et al, 1997), and the meta-analysis results were updated from three further trials (Angus et al, 1996; Avdeev et al, 1998; Celikel et al, 1998).

**Sources searched to identify primary studies**
The original meta-analysis was characterised by a comprehensive literature search (including a search of MEDLINE), explicit selection criteria, critical appraisal of studies and data synthesis of RCT results.

**Criteria used to ensure the validity of primary studies**
The criteria used to ensure the validity of primary studies were not reported in this paper. Please refer to the original meta-analysis, Keenan et al, 1997 (see below in Other Publications of Related Interest).

**Methods used to judge relevance and validity, and for extracting data**
The authors’ criteria used to ensure the validity of primary studies were not stated in this paper.

**Number of primary studies included**
For the hospital survival and intubation outcomes, a meta-analysis and a further three primary studies were used. These studies and those included within the meta-analysis were randomised controlled trials (RCTs).

Data for the timing and probability of interventions, such as intubation, and side effects, such as ventilation-associated pneumonia (VAP), were taken from the literature review (see above). More than fourteen studies were used.

**Methods of combining primary studies**
Meta-analysis was carried out to combine the primary studies to derive the primary outcome measures.

**Investigation of differences between primary studies**
This study did not report the differences found between the primary studies in the meta-analysis. Users are referred to the original articles. The authors stated that the studies related to the patient population in question in this study.

**Results of the review**
The pooled risk difference of the effect of NPPV on the need for intubation was -0.337 (95% CI: -0.523 to -0.231).

The pooled risk difference of the effect of NPPV on hospital mortality was -0.161 (95% CI: -0.248 to -0.0754).

**Measure of benefits used in the economic analysis**
A cost-consequences analysis was undertaken. Please see the effectiveness results reported above.

**Direct costs**
Quantities and resources were reported separately. Direct costs were based on the cost of a day in different care settings within the hospital. The direct costs used within the study were: intensive care unit (ICU) with and without pneumonia, for conventional ventilation and conventional plus NPPV; transitional care unit (TCU) with or without NPPV; day in a ward post ICU/TCU; and last two days in a ward before discharge.
Resource use data, such as the time spent in different types of hospital units, were taken from a variety of sources including studies published between 1986 and 1996, and from a regional database of admissions to teaching hospitals’ ICUs.

Cost data were taken from the Transition 1 case-costing system from the hospital. This costs an inpatient day based on the various inputs used and includes apportioning of hospital overheads. Costs available from the system included nurse time, allied healthcare professional time, laboratory, radiology, pharmacy, nutrition and ventilation costs. One-off costs, or costs not included within the system, were applied separately, as were pneumonia-related costs and costs of planning and discharge. The unit prices used for these costs were not stated. The costs used were average costs rather than marginal or incremental costs. Physician costs, other costs to the healthcare system incurred outside the hospital, and direct costs to families and patients were not included.

A decision tree model was used to cost each of the possible patient pathways. Costs were then rolled back to derive the expected costs of treatment with and without NPV.

Discounting was not performed as all costs (and benefits) were incurred within the first year. The price year used was 1996.

**Statistical analysis of costs**

Costs and resources were treated as point estimates. In other words, the data were treated deterministically. Consequently, no statistical tests were undertaken but sensitivity analysis was performed.

**Indirect Costs**

Indirect costs were not included in the analysis as the perspective was that of the hospital only.

**Currency**

Canadian dollars (Can$).

**Sensitivity analysis**

One way and two way sensitivity analysis of cost was undertaken on the following parameters:

- patients requiring early or late intubation in the standard therapy arm;
- patients requiring prolonged ventilation once intubated;
- incidence of VAP;
- length of stay on a general ward;
- quantity of respiratory technologist time required for NPPV;
- location of patients at hospital admission (intermediate care unit or ICU).

**Estimated benefits used in the economic analysis**

The authors did not summarise the relative clinical benefits of using NPV therapy. However, they did show that it was more effective than standard therapy and the reader is therefore referred to the effectiveness results reported above.

**Cost results**

The cost of standard therapy was Can$10,455 per patient. The cost of standard therapy plus NPV was Can$7,211. This represents a cost saving of Can$3,244 through using NPV.
These costs included the cost of dealing with any side effects during treatment such as VAP. These costs were the average expected costs of treating a patient with the two treatments. No costs were discounted as all were incurred within one year.

**Synthesis of costs and benefits**
Costs and benefits were not combined as the intervention (use of NPPV) was the dominant strategy. In other words, use of NPPV provided more benefits at a lower cost than just standard treatment.

Cost savings were sensitive to intubation rates and period of ventilation once intubated. Standard therapy was cheaper when intubation rates were comparable between the two strategies at around 30 - 35%. Cost savings decreased noticeably when the probability of having prolonged ventilation was decreased towards zero for both strategies. Changing to an ICU setting increased total costs in each arm, but the cost difference remained similar.

**Authors’ conclusions**
The use of NPPV for severe, acute exacerbation of COPD is more effective and less expensive than standard therapy, when viewed from the perspective of the hospital. NPPV decreases both the risk of intubation and mortality and costs the hospital less per admission.

**CRD COMMENTARY - Selection of comparators**
The choice of comparator was justified as it was standard therapy, i.e. the treatment that patients would have received in the absence of NPPV. The reader should decide if the standard therapy described above is used in his or her own setting.

**Validity of estimate of measure of effectiveness**
The effectiveness evidence was taken from a published meta-analysis updated with recent trials. Methods, such as using RCTs and performing a systematic search of the literature, were used to reduce the probability of bias in estimating effectiveness. It is not clear to what extent the authors accounted for heterogeneity, for example by fixed or random effects modelling in the meta analysis, since the details are in another publication. One concern is that the authors implicitly assumed that varying the parameters in the model would only impact on costs and not on effectiveness. If there were a correlation between this and the choice of NPPV and standard therapy or standard therapy alone, it is therefore conceivable, that effectiveness differences could be in the other direction.

**Validity of estimate of measure of benefit**
Two health outcome measures were used: hospital mortality and intubation rates. As the intervention was dominant for both measures, it was not necessary to combine them into a single health outcome. The authors commented that this patient group had a relatively short project life span and had marked disability. Consequently, using measures such as quality-adjusted life years would reduce the benefits of both treatment arms. However, NPPV would still continue to provide more benefits, primarily through lower hospital mortality.

**Validity of estimate of costs**
All the costs included were appropriate for the hospital perspective taken by the authors. However, readers should be aware that physician costs were excluded from this study. Such costs would normally be included under a hospital perspective within the UK. However, if physician costs were likely to be the same between the two alternatives, the omission of these costs would not affect the final conclusion and the magnitude of cost savings reported. Costs and quantities were reported separately.

One off costs and costs of admission and discharge were not reported. However, these costs were unlikely to be the cost drivers when compared to the daily costs calculated and so would only have had a relatively small impact on the overall results if had they been varied in the sensitivity analysis.
Resource use data were taken from published sources and sensitivity analysis was performed on several parameters affecting resource use. The ranges used in the sensitivity analysis seem appropriate for each parameter.

1996 prices were used and were taken from the authors' setting using a commercially available costing system. This system calculated the costs of providing care rather than prices charged. A statistical analysis of the prices used was not performed. Since all costs were incurred over one year discounting was unnecessary.

**Other issues**
Comparisons of findings with other studies was not necessary as the effectiveness data were taken from a meta-analysis and this was the first economic evaluation providing a rigorous evaluation of costs of NPPV for this patient group.

The authors did not discuss the generalisability of their results to other settings. However, the effectiveness data used implied that the outcomes were generalisable to other countries and the explicit description of resources and costs used should allow the reader to calculate expected costs in their own settings if sufficient data is available. Results were not presented selectively and the authors' conclusions reflected accurately the scope of the analysis. However, readers should refer to the comments in accompanying editorial to the original paper.

The authors reported a number of limitations to their study. In particular, the results related to patients with severe, acute exacerbation of COPD who developed respiratory failure. They commented that milder conditions were likely to reduce the potential cost savings and effectiveness as intubation rates were less likely, the need for NPPV was less and lengths of stay were likely to be more similar across the two groups.

**Implications of the study**
The authors concluded that NPPV should be used alongside standard treatment for patients with acute, severe exacerbations of COPD. However, they warned against using their results to conclude that NPPV is also cost-effective for patients with milder symptoms. The cost-effectiveness of treating milder conditions needs to be evaluated further. Decision makers in each local setting should assess the risk and benefits of using NPPV in their own environment.

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**Other publications of related interest**


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