Noninvasive ventilation in acute respiratory failure: a meta-analysis update

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Authors' objectives
To present a meta-analytic update on the effects of noninvasive ventilation (NIV) in the management of acute respiratory failure, with the primary objective to address the role of NIV in reducing mortality in patients presenting with acute respiratory failure secondary to chronic obstructive pulmonary disease (COPD) exacerbations and other non-COPD parenchymal processes.

Searching
MEDLINE was searched from 1966 to 2000 on two separate occasions using the following search terms: 'respiratory failure/insufficiency', 'obstructive lung disease', 'ventilation', 'intermittent positive pressure ventilation' and 'mechanical ventilation'. In addition, a manual search and review of leading specific journals, focusing on abstracts of scientific forums, was undertaken for the period 1989 to 2000. The journals reviewed were American Journal of Respiratory and Critical Care Medicine, Chest, Critical Care Medicine, European Respiratory Journal, Intensive Care Medicine, and Thorax. The bibliographies of reviews and articles were examined for other articles on NIV in respiratory failure.

The makers of BiPAP were contacted for other trials of NIV in respiratory failure (see Other Publications of Related Interest no.1). In addition, information was obtained from a recent International Consensus Conference on NIV (see Other Publications of Related Interest no.2).

Study selection
Study designs of evaluations included in the review
Prospective randomised controlled clinical trials (RCTs) were included.

Specific interventions included in the review
The use of NIV compared with standard medical therapy. Studies relating to the following were excluded: the use of NIV in weaning and post-extubation, post-operative NIV, and NIV compared with mechanical ventilation (MV). The included studies involved either pressure-cycled ventilation or volume-cycled ventilation.

Participants included in the review
Patients presenting with acute respiratory failure. Studies on cardiogenic pulmonary oedema were excluded as were those of NIV in specialised or alternate populations, e.g. cancer patients, solid organ transplant, children, obstructive sleep apnoea, post-operative asthma and congestive cardiac failure. The included studies were categorised into those that examined COPD exacerbations only (COPD group), or those that examined respiratory failure of diverse aetiology (i.e. pneumonia, interstitial lung disease, and other parenchymal processes) and included COPD patients who had respiratory failure secondary to other cardiopulmonary disease processes (mixed group). The included trials involved COPD exacerbations, pneumonia, associated heart failure, and non-COPD parenchymal processes.

Outcomes assessed in the review
The primary outcome was mortality. The secondary outcomes were the need for MV and the length of hospital stay.

How were decisions on the relevance of primary studies made?
The authors do not state how the papers were selected for the review, or how many of the reviewers performed the selection.

Assessment of study quality
The following features of quality were assessed: the mode of randomisation (method, concealment), definition of inclusion and exclusion criteria, objective criteria for intubation, cointerventions, follow-up details, complication rates, and intention-to-treat analysis. Three investigators jointly reviewed the included studies, and any differences of opinion
were settled by consensus.

**Data extraction**
The authors do not state how the data were extracted for the review, or how many of the reviewers performed the data extraction. The following categories of data were extracted from each study: study reference and publication details; country; the number of patients in the NIV and control groups; the type of participants (e.g. COPD or mixed); whether the inclusion and exclusion criteria were defined; the mode of randomisation used; the interface used; the type of NIV used; ventilator type; whether predefined intubation criteria were used; whether details on MV were provided; whether information on drop-outs was reported; and whether complications were reported.

**Methods of synthesis**
*How were the studies combined?*
The random-effects estimator of DerSimonian and Laird was used to for the assessment of treatment effects, as heterogeneity of the treatment effects was diagnosed.

Publication bias was visually assessed using the funnel plot (see Other Publications of Related Interest no.3) and then formally checked by the rank correlation test of Begg and the regression-based test of Egger (see Other Publications of Related Interest no.4). These tests were supplemented by the 'trim and fill' method (see Other Publications of Related Interest nos.5-6).

*How were differences between studies investigated?*
Heterogeneity was diagnosed using the Q test (see Other Publications of Related Interest no.7) at a p-value of less than or equal to 0.1, and supplemented by the L'Abbe plot (see Other Publications of Related Interest no.8).

**Results of the review**
There were 15 RCTs involving 405 NIV patients and 388 standard medical therapy patients. Eight RCTs related to COPD groups and seven related to mixed groups.

As there was underlying heterogeneity of the treatment effects, only the random-effects model was used.

**All studies.**

- **Mortality (14 studies):** NIV was associated with a reduction in mortality; the overall risk difference was -0.08 (95% confidence interval, CI: -0.16, -0.01, p=0.03).

- **MV (12 studies):** NIV was associated with a reduced need for MV; the overall risk difference was -0.19 (95% CI: -0.28, -0.09, p=0.01).

- **Hospital length of stay (10 studies):** NIV was associated with a shortened length of stay; the overall weighted mean difference was -2.74 (95% CI: -4.59, -0.89, p=0.004).

**COPD studies.**

- **Mortality (7 studies):** NIV was associated with reduction in mortality; the overall risk difference was -0.13 (95% CI: -0.21, -0.06, p=0.001).

- **MV (6 studies):** NIV was associated with a reduced need for MV; the overall risk difference was -0.18 (95% CI: -0.33, -0.03, p=0.03). Hospital length of stay (5 studies): NIV was associated with a shortened length of stay; the overall weighted mean difference was -5.66 (95% CI: -10.10, -1.23, p=0.01).

**Mixed studies.**

- **Mortality (7 studies):** there was no demonstrable reduction in mortality; the overall risk difference was 0.00 (95% CI:
MV (6 studies): NIV was associated with a reduced need for MV; the overall risk difference was -0.20 (95% CI: -0.32, -0.08, p=0.001). Hospital length of stay (5 studies): there was no demonstrable reduction in the length of stay; the overall weighted mean difference was -0.74 (95% CI: -2.78, 1.30).

Publication bias: the funnel plot suggested missing studies. However, Begg's test (z=0.33, p=0.78) and Egger's test (slope coefficient -0.14, p=0.2) failed to demonstrate publication bias, as did the 'trim and fill' method.

Further results relating to complication rates; the effect of predefined confounders on treatment effect; and treatment effects as a function of baseline risk, COPD versus mixed subgroups, and published versus unpublished trials, were available from the study.

Authors' conclusions
Substantial reductions in mortality and the need for subsequent MV were associated with NIV in acute respiratory failure, especially in the COPD subgroup. The effect on hospital length of stay was variable. Heterogeneity of the treatment effects was observed.

CRD commentary
The objective of the study was clearly set out and well supported by a priori eligibility criteria. Only one database (MEDLINE) was searched, but the search terms and dates were well reported and various other sources were also searched. It was not, however, reported whether any publication or language restrictions were applied and, therefore, relevant studies may have been missed. Quality features of the included studies were assessed, but not all the results for this were reported. The data analysis used a suitable quantitative synthesis, and heterogeneity and publication bias were investigated. Details of the review process for the inclusion or exclusion of studies and the data extraction were not reported. The authors' conclusions appear to follow on from the findings, but should be considered in light of the limitations mentioned.

Implications of the review for practice and research
Practice: The authors state that, although this meta-analysis suggested a strong benefit with the use of NIV in the COPD exacerbation group, caution must be exercised when translating this to routine practice in all COPD patients who present with respiratory failure.

Research: The authors state that it is possible that the beneficial effects of NIV may have been offset by delayed or prolonged NIV in some subgroups of patients, and this needs to be studied further. They also state that further studies are needed to establish the role of NIV in the diverse mixed group of patients.

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Other publications of related interest

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**Record Status**
This is a critical abstract of a systematic review that meets the criteria for inclusion on DARE. Each critical abstract contains a brief summary of the review methods, results and conclusions followed by a detailed critical assessment on the reliability of the review and the conclusions drawn.