Authors' objectives
To assess the level of evidence available to support the use of noninvasive positive pressure ventilation (NPPV) in patients with acute respiratory failure.

Searching
The search strategy included a review of personal files, a review of bibliographies of all relevant articles retrieved, and one or more searches using the computerised database MEDLINE (from 1966 to May 1997). Within each diagnostic group, the initial search included the terms 'randomized controlled trials' (pt) or 'controlled clinical trials' or 'clinical trials, randomized'. When two or more RCTs were identified within a diagnostic group, no further searches were performed. If less than two RCTs were identified, a further search was conducted without the terms related to randomisation.

The following keywords were used to search for primary ventilatory failure: 'respiratory insufficency/failure' (explode) or 'lung disease, obstructive' (explode) AND 'human' (mh) AND 'ventilation, mechanical' (explode) or 'ventilators, mechanical' (explode) or 'intermittent positive pressure ventilation' or 'inspiratory positive positive pressure ventilation'. For primary hypoxic failure the keywords used included: 'noninvasive ventilation' combined individually with the keywords 'pneumonia, ARDS, cardiogenic pulmonary edema, pulmonary hemorrhage, pulmonary hypoexemia' and 'review'.

Study selection
Study designs of evaluations included in the review
Randomised controlled trials (RCTs) or controlled clinical trials. In the absence of such study designs other studies (such as historical controls and case series) were also considered.

Specific interventions included in the review
NPPV and control (i.e. standard therapy).

Participants included in the review
Patients suffering from acute respiratory failure. Patients were divided into the following two categories:

1. Those presenting with primary ventilatory failure.
2. Those presenting with a primary problem of gas exchange (hypoxemic failure).

The second category was composed of those patients who secondarily develop ventilatory failure, and those with solely hypoxic failure. Patients generally presented with primary ventricular failure as a result of either an increase in airways resistance (chronic obstructive pulmonary disease (COPD) or asthma) or an acute impairment of respiratory muscle function (e.g. Guillain-Barre syndrome or myasthenia gravis).

Outcomes assessed in the review
Hospital survival, need for endotracheal intubation, and 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 authors performed the selection.

Assessment of study quality
A validity assessment was only applied to RCTs, which included the following criteria: randomisation concealed, objective criteria for study population, objective criteria for need for intubation, complete follow-up, listing of potential confounders, mention of cointerventions, intention-to-treat analysis. The authors do not state how the papers were assessed for validity, or how many of the authors performed the validity assessment.

**Data extraction**
The authors do not state how the data were extracted for the review, or how many of the authors performed the data extraction.

**Methods of synthesis**

How were the studies combined?
When the results lent themselves to statistical pooling a meta-analysis was conducted (the statistical method used was not stated); otherwise, results were summarised in a qualitative fashion. Pooled data was presented as odds ratios (OR) with 95% confidence intervals (CI). A level of evidence, as suggested by Cook and colleagues (see Other Publications of Related Interest), that supports the use of NPPV for acute respiratory failure was assigned to each setting.

How were differences between studies investigated?
No statistical test for heterogeneity was conducted, however the author's comments regarding statistical pooling suggest that some form of heterogeneity assessment was carried out.

**Results of the review**

Eight RCTs and 3 case series were included in the analysis of primary ventilation failure (7 RCTs included patients with COPD (number of patients not stated) and 1 RCT and 3 case series included patients presenting with an asthmatic attack (n=28)). One RCT and 14 case series were included in the analysis of primary hypoxic failure for the population as a whole (for individual diagnostic categories, 7 case series reported data on patients presenting with pneumonia (n=36); 5 case series reported data on patients with acute respiratory distress syndrome (n=15); and 1 RCT, 5 case series and 2 case reports presented data on patients with cardiogenic pulmonary edema (n=22)).

**Primary ventilation failure:**

**NPPV in COPD.**

For patients presenting with acute exacerbation of COPD, pooled data from 6 RCTs showed a decrease in hospital mortality and need for endotracheal intubation (OR 0.22, 95% CI: 0.09, 0.54; OR 0.12, 95% CI: 0.05, 0.29 respectively). Hospital length of stay could not be statistically pooled, and of the three RCTs that presented data on this outcome only one RCT found the length of hospital stay to be statistically shorter for the NPPV-treated group. One further RCT included milder presentations COPD (n=24). None of the patients required intubation and no difference was found in hospital length of stay between NPPV and standard therapy.

There was level 1 evidence to support the use of NPPV in severe acute exacerbation of COPD. Trial evidence was lacking to support the use of NPPV in milder COPD exacerbations.

**NPPV in patients with asthmatic attack**

In one RCT none of the patients required intubation, and two patients in each group were admitted to hospital with no data available on length of stay. Two emergency room physicians were responsible for enrolling patients, and no mention was made of randomisation concealment. Three case series suggested a decrease in the need for endotracheal intubation (total number requiring intubation = 7).

There was only level 5 evidence to support the use of NPPV in patients with severe asthmatic attacks.

No studies were found that assessed the use of NPPV in patients with acute ventilatory failure owing to neuromuscular diseases.
Primary Hypoxic failure:

1 RCT that included patients with acute respiratory failure of multiple causes found that, although patients treated with NPPV had slight reductions in the need for intubation (OR 0.70, 95% CI: 0.16, 3.07), hospital survival (OR 0.51, 95% CI: 0.12, 2.10), and intensive care unit length of stay (17 + or - 19 versus 25 + or - 23 days, p=0.16) compared to those treated conventionally, none of these reductions reached statistically significance.

There was only level 2 (insufficient) evidence to support the use of NPPV in hypoxemia respiratory failure.

NPPV in pneumonia.

According to 7 case series, which included 36 patients with pneumonia, the total intubation rare was 10 (28%, range 0-100) and the total mortality was 10 (28%, range 0-50).

There was insufficient evidence to support the use of NPPV in patients with acute respiratory failure owing primarily to pneumonia.

NPPV in acute respiratory distress syndrome (ADRS).

According to 5 uncontrolled case series, that included 15 patients with ADRS, eight (53%) required endotracheal intubation, and there were six deaths (40%).

There was only level 5 evidence to support NPPV in patient with ARDS.

NPPV in Cardiogenic Pulmonary Edema.

Only one RCT investigated the use of NPPV for patients with acute cardiogenic pulmonary edema. 14 patients were randomised to receive NPPV and 13 received continuous positive airway pressure (CPAP). There was no significant difference between the two groups with respect to intubation requirements, intensive care unit length of stay, hospital length of stay, or mortality. However, there was a clinically significant difference between the two groups at baseline, with the NPPV having a more seriously ill population. According to 7 uncontrolled studies, that included 22 patients with cardiogenic pulmonary edema, 7 (32%) required endotracheal intubation, 3 (14%) died.

There was insufficient evidence in the literature to support the use of NPPV in patients with cardiogenic pulmonary edema.

Authors' conclusions

From our systematic review of the literature, we were able to identify numerous studies describing the use of NPPV in patients with acute respiratory failure; however, most of these studies were in the form of case reports or case series. The potential for selection bias and the inability to discern the effect of NPPV alone on outcome without an appropriate control group precludes strong inferences about the impact of NPPV. We believe that there is currently good evidence to support the use of NPPV in patients with severe COPD exacerbations. Use of NPPV in milder COPD exacerbations needs further study. Beyond the COPD population, there is currently insufficient evidence to support the use of NPPV in acute respiratory failure.

CRD commentary

The review includes a clearly stated objective and inclusion criteria, and also assesses the validity of included controlled trials. However, very little information is presented on the findings of the validity assessment and there is limited data presented on individual studies, especially for case series. The literature search is rather limited, as the only electronic database that was searched was MEDLINE, which means that some relevant information may have been missed. The search strategy relating to primary hypoxic failure seems to be less thorough than the one conducted for primary ventilatory failure. The authors’ conclusions seem to follow from the results.
Implications of the review for practice and research
The authors state that further RCTS are needed to support the use of NPPV in patients with acute respiratory failure owing to severe asthmatic attacks, pneumonia, ARDS, and cardiogenic pulmonary edema.

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Other publications of related interest

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