



## reviews

# Acute Applications of Noninvasive Positive Pressure Ventilation\*

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Noninvasive positive-pressure ventilation (NPPV) has been used increasingly to treat acute respiratory failure (ARF). The best indications for its use are ARF in patients with COPD exacerbations, acute pulmonary edema, and immunocompromised states. For these indications, multiple controlled trials have demonstrated that therapy with NPPV avoids intubation and, in the case of COPD and immunocompromised patients, reduces mortality as well. NPPV is used to treat patients with numerous other forms of ARF, but the evidence is not as strong for its use in those cases, and patients must be selected carefully. The best candidates for NPPV are able to protect their airway, are cooperative, and are otherwise medically stable. Success is optimized when a skilled team applies a well-fitted, comfortable interface. Ventilator settings should be adjusted to reduce respiratory distress while avoiding excessive discomfort, patient-ventilator synchrony should be optimized, and adequate oxygenation should be assured. The appropriate application of NPPV in the acute care setting should lead to improved patient outcomes and more efficient resource utilization.

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**Key words:** acute respiratory failure; COPD; mechanical ventilation; noninvasive ventilation; pulmonary edema

**Abbreviations:** CPAP = continuous positive airway pressure; DNI = do not intubate;  $FI_{O_2}$  = fraction of inspired oxygen; NPPV = noninvasive positive-pressure ventilation

Standard therapy for acute respiratory failure that is unresponsive to conservative medical therapy often requires the intervention of mechanical ventilation via an endotracheal tube. However, endotracheal intubation poses a risk of morbidity, including upper airway trauma, nosocomial pneumonia, and sinusitis. In addition, endotracheal intubation may prolong ICU and hospital stays, as additional time may be necessary for weaning from ventilation and the treatment of

complications.<sup>1-3</sup> The potential benefit of continuous positive airway pressure (CPAP) using a face mask in patients with acute respiratory failure was recognized decades ago.<sup>4,5</sup> In more recent years, noninvasive positive-pressure ventilation (NPPV) [*ie*, the combination of pressure support and positive end-expiratory pressure delivered via a face mask or nasal mask] has been used increasingly to avoid endotracheal intubation and its attendant complications in patients with acute respiratory failure. Evidence has rapidly accumulated to support many of these applications, and the strength of this evidence for different causes of acute respiratory failure is summarized in Table 1. The purpose of this review is to provide an update on the status of this evidence, to make recommendations on guidelines for the use of NPPV in the acute setting, and to offer practical suggestions on how to maximize success.

### EVIDENCE FOR EFFICACY

#### Obstructive Lung Diseases

**COPD:** The most studied application of NPPV is for acute exacerbations of COPD. Just over a dozen

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**Table 1—Evidence To Support Use of NPPV for Different Types of Acute Respiratory Failure**

Type of Evidence	Evidence
Strong (multiple controlled trials)	COPD exacerbations Acute cardiogenic pulmonary edema* Immunocompromised patients Facilitation of weaning in COPD patients
Less strong (single controlled trial or multiple case series)	Asthma Cystic fibrosis Postoperative respiratory failure Avoidance of extubation failure DNI patients
Weak (few case series or case reports)	Upper airway obstruction Acute respiratory distress syndrome (ARDS) Trauma Obstructive sleep apnea, obesity hypoventilation

\*Evidence strongest for CPAP.

years ago, Brochard et al<sup>6</sup> showed that pressure support ventilation, administered via a face mask, significantly reduced the need for intubation, the duration of mechanical ventilation, and ICU length of stay compared to historically matched control

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subjects. Subsequently, six randomized controlled trials have confirmed these findings<sup>7-13</sup> (Table 2). Bott et al<sup>7</sup> randomized 60 patients who had exacerbations of COPD with similar degrees of baseline arterial blood gas abnormalities to receive conventional therapy or conventional therapy plus volume-limited ventilation via a nasal mask. Bronchodilators were administered by nebulizer, and an equal percentage of patients in both groups received therapy with both corticosteroids and antibiotics. The NPPV group had significantly greater improvements in PaCO<sub>2</sub> as well as dyspnea scores within the first hour. Also, there was a 10% mortality rate in the NPPV

group compared to 30% in control subjects but this was not statistically significant unless four patients who had been randomized to NPPV, but did not actually receive it, were excluded from the analysis.

In their subsequent randomized trial on 31 patients with hypercapnic respiratory failure, Kramer et al<sup>8</sup> found that the incidence of endotracheal intubation was reduced from 67% in control subjects to 9% in the NPPV-treated COPD subgroup. Despite having similar baseline vital signs, arterial blood gas abnormalities, and APACHE (acute physiology and chronic health evaluation) scores, this study showed more rapid improvements in respiratory rates and blood gas levels in the NPPV group but no significant differences in hospital lengths of stay or mortality rates, perhaps because of the small sample size. In their multicenter trial, Brochard et al<sup>9</sup> randomized 85 patients with hypercapnic respiratory failure due to COPD to receive face mask pressure support ventilation or standard therapy alone. Both groups had similar baseline vital signs, arterial blood

**Table 2—Randomized Control Trials Using NPPV in Acute Respiratory Failure Caused by COPD**

Study/Year	Patients, No.		Mean PaCO <sub>2</sub> , mm Hg		Failures, No. (%)†		p Value
	NPPV Group	Control Group	Pre-NPPV	Post-NPPV*	NPPV Group	Control Group	
Bott et al <sup>7</sup> /1993	30	30	65	55	3 (10)	9 (30)	0.014
Kramer et al <sup>8</sup> /1995‡	16	15	74	67	5 (31.1)	11 (73.3)	< 0.05
Brochard et al <sup>9</sup> /1995‡	43	42	70	68	11 (25.6)	31 (73.8)	< 0.001
Angus et al <sup>10</sup> /1996	9	8	76	65	0 (0)	3 (37.5)	Not given
Celikel et al <sup>11</sup> /1998	15	15	69	64	1 (6.6)	6 (40)	< 0.05
Plant et al <sup>12</sup> /2000	118	118	66	61	18 (15.3)	32 (27.1)	0.02
Barbe et al <sup>13</sup> /1996	14	10	59		4 (28.6)	0 (0)	Not given

\*Post-NPPV values obtained 45 min to 3 h after initiation of NPPV.

†Including patients who were intubated, failed to tolerate the mask, or died.

‡Included some patients without COPD.

gas abnormalities, and simplified acute physiology scores. This trial not only showed that vital signs, blood gas values, and encephalopathy scores improved more rapidly in the NPPV-treated group than in control subjects, but also that intubation rates (from 74 to 26%), hospital lengths of stay (from 35 to 17 days) and mortality rates (from 31 to 9%) improved significantly. In addition, total complication rates (most notably pneumonia and other complications from endotracheal intubation) were significantly reduced (from 48 to 16%). Although the use of nebulized bronchodilators was the same in both groups, this study has been criticized for using high supplemental oxygen rates ( $\leq 5$  L/min) in the control group, which may have predisposed these subjects to a high intubation rate,<sup>14</sup> but the relatively large number of patients and prospective randomized design are important strengths of the study. A smaller subsequent trial<sup>11</sup> also found significant reductions in intubation rates as well as reduced hospital lengths of stay (from 14.6 to 11.7 days;  $p < 0.05$ ) among NPPV-treated patients compared to control subjects. The remarkably high success rate for NPPV-treated patients in this trial (93%) was attributed to the early institution of therapy with NPPV.

In the largest randomized trial, Plant et al<sup>12</sup> treated 236 patients with acute exacerbations of COPD with NPPV or standard therapy administered by nurses in general medical respiratory wards. Baseline patient characteristics (including age, vital signs, and gas exchange abnormalities) were similar in both groups, and medical management was standardized (including therapy with nebulized bronchodilators, corticosteroids, and antibiotics) for all patients. The intubation and mortality rates were significantly lower in the NPPV group compared to the control group (15% vs 27% [ $p = 0.02\%$ ] and 10% vs 20% [ $p = 0.05$ ], respectively). Once again, the authors found more rapid improvements in arterial pH, respiratory rate, and breathlessness in the NPPV group compared to the control group. Of note, the mortality benefit was not apparent in patients with a pH of  $< 7.30$ , and the authors recommended that this latter more severely ill subgroup be treated in the ICU rather than on a general medical ward.

The only randomized trial to obtain negative findings<sup>13</sup> divided 24 patients with COPD exacerbations between NPPV and standard therapy groups. Four of the 14 patients who initially had been randomized to therapy with NPPV were excluded due to intolerance. Although NPPV failed to lower the intubation or mortality rates or hospital length of stay in this study, it is notable that no intubations or mortalities occurred in the control group. Furthermore, the

hospital length of stay was only one third that of the control group in the study of Brochard et al.<sup>9</sup> Thus, the enrolled patients appeared to be less severely ill than those included in other randomized trials and were less likely to benefit from NPPV. Perhaps the most important conclusion to be drawn from the negative trial<sup>13</sup> is that patients with relatively mild COPD exacerbations are not likely to benefit from NPPV.

Taken together, the above studies provide strong evidence to support the contention that NPPV is effective therapy in patients with acute COPD exacerbations, not only bringing about rapid symptomatic and physiologic improvements, but also significantly reducing the need for intubation, mortality rates, and, in some studies, hospital lengths of stay. In addition, although the use of NPPV was associated with nasal bridge ulceration in  $\leq 46\%$  of patients and gastric distension occurred occasionally,<sup>11</sup> major complications such as aspiration were very infrequent, and overall complications were significantly reduced in some of the studies.<sup>9</sup> A meta-analysis<sup>15</sup> of these studies also concluded that NPPV significantly reduces the need for intubation and mortality rates compared to conventional therapy. Based on this evidence, consensus groups of expert clinicians have recommended that NPPV be considered the ventilatory mode of first choice in selected patients experiencing COPD exacerbations.<sup>16</sup>

*Asthma:* The success of NPPV in treating COPD patients raises the possibility that it would also be beneficial in those with acute asthma. However, no randomized controlled trials have confirmed this hypothesis. Furthermore, the pathophysiologies and natural histories of the two entities differ markedly, and, thus, it is not fair to assume that one would respond to NPPV in the same way as the other. However, cohort studies<sup>17,18</sup> have reported successful outcomes with NPPV in patients with severe status asthmaticus that is complicated by CO<sub>2</sub> retention. In one study,<sup>18</sup> only 2 of 17 asthmatic patients required intubation after starting therapy with NPPV, with PaCO<sub>2</sub> falling from an average of 65 to 52 mm Hg and the respiratory rate falling from 29 to 20 breaths/min ( $p = 0.002$  and  $0.0001$ , respectively), after 2 h of therapy. In a retrospective analysis<sup>19</sup> of 33 asthmatic patients who were deemed to be candidates for NPPV, the outcomes of 11 patients managed with invasive mechanical ventilation were compared with 22 who had been managed noninvasively. The NPPV patients were less hypercapnic than those who were managed invasively, but gas exchange and vital signs improved rapidly in the NPPV group, and only three patients eventually required endotracheal intubation. A randomized

controlled trial<sup>20</sup> on the use of NPPV in patients with acute asthma found no significant advantages attributable to the use of NPPV. However, the study was severely underpowered, and the authors reported that bias on the part of emergency department physicians favoring NPPV interfered with study enrollment because of the concern that enrolled patients might become control subjects and not receive NPPV therapy.<sup>20</sup>

Thus, the evidence supporting the use of NPPV in patients with acute severe asthma is inconclusive. However, a trial of NPPV in carefully selected and monitored patients is justifiable based on the anecdotal evidence. While no selection guidelines have been established, a reasonable approach would be to use NPPV in patients who fail to respond promptly to standard initial medical therapy, but who have not developed contraindications to NPPV (see "Patient Selection" section). Caution is advised because the condition of an asthmatic patient may deteriorate abruptly, and the delay of needed intubation is a risk. Some authors<sup>21</sup> have indicated that aerosolized medication may be more effectively delivered via the noninvasive ventilation circuit compared to a standard nebulizer, and, anecdotally, NPPV has been combined with heliox to treat status asthmaticus (personal observation), although the administration of heliox via mask ventilation has not been standardized and no data are available to support this practice.

**Cystic Fibrosis:** A few anecdotal reports<sup>22,23</sup> support the use of NPPV therapy in patients with acute exacerbations of cystic fibrosis. Hodson et al<sup>22</sup> used NPPV to treat six cystic fibrosis patients with baseline FEV<sub>1</sub> values ranging from 350 to 800 mL who developed acute CO<sub>2</sub> retention superimposed on chronic CO<sub>2</sub> retention. These patients, whose initial PaCO<sub>2</sub> values ranged from 63 to 112 mm Hg, received NPPV for periods ranging from 3 to 36 days. Four patients survived until a heart-lung transplantation could be performed. These same investigators recently reported<sup>23</sup> their experience using NPPV in 113 cystic fibrosis patients who had experienced acute deteriorations. Of the 90 patients (median FEV<sub>1</sub>/FVC ratio, 0.5 L) who were either on or being evaluated for the lung transplant waiting list, 28 patients had successfully received lung transplantation and 10 others were still on the list. The authors noted that NPPV improved hypoxia but not hypercapnia. These case series suggest that NPPV is helpful as a rescue therapy in supporting acutely deteriorating cystic fibrosis patients, providing a bridge to transplantation.

**Upper Airway Obstruction:** NPPV can be used to treat patients with upper airway obstructions such as that caused by glottic edema following extubation. In

this situation, NPPV can be combined with aerosolized medication and/or heliox, but to date no controlled trials have demonstrated the efficacy of this approach. However, it should be noted that all ventilators may not have the capability to add heliox. If therapy with NPPV is considered, patients should be selected with great caution and monitored closely because upper airway obstruction can lead to precipitous deteriorations. The inappropriate use of NPPV in patients with tight, fixed upper airway obstruction should be avoided so as not to delay the institution of definitive therapy.

**Acute Respiratory Failure Due to Obstructive Sleep Apnea:** Patients with acute-on-chronic respiratory failure caused by severe sleep apnea syndrome have been treated with NPPV and have been transitioned to CPAP once they are stabilized,<sup>24</sup> but no controlled trials have evaluated this application.

#### HYPOXEMIC RESPIRATORY FAILURE

The term *hypoxemic respiratory failure* refers to a subgroup of patients whose acute respiratory failure is characterized by severe hypoxemia (*ie*, PaO<sub>2</sub>/fraction of inspired oxygen [FIO<sub>2</sub>] ratio,  $\leq 200$ ), severe respiratory distress (*ie*, respiratory rate,  $> 35$  breaths/min), and a non-COPD diagnosis including pneumonia, ARDS, trauma, or cardiogenic pulmonary edema.<sup>17</sup> Studies on this subgroup of patients have yielded conflicting results. Meduri et al<sup>25</sup> have reported success with NPPV in all four patients with hypoxemic respiratory failure in their early trial. Later, however, Wysocki et al<sup>26</sup> observed no significant benefit that was attributable to NPPV among patients with hypoxemic respiratory failure, unless patients were hypercapnic. In a large, uncontrolled series of 158 patients with various forms of respiratory failure who had been treated with NPPV, Meduri et al<sup>17</sup> identified 41 with hypoxemic respiratory failure, 66% of whom avoided endotracheal intubation. Subsequently, Antonelli et al<sup>27</sup> randomized 64 patients with hypoxemic respiratory failure to receive therapy with NPPV or prompt intubation. Baseline characteristics including the PaO<sub>2</sub>/FIO<sub>2</sub> ratio (which was approximately 120) and therapies for the conditions precipitating the respiratory failure were similar in both groups, with the exception of baseline pH, which was lower in control subjects than in the NPPV group (7.37 vs 7.45, respectively;  $p = 0.002$ ). NPPV was as effective as invasive mechanical ventilation in improving oxygenation within the first hour, and only 10 of the 32 NPPV patients required intubation. Patients in the NPPV group had significantly fewer septic complications, and exhibited strong trends toward shorter stays in the ICU

and lower mortality rates. In another randomized trial of patients with various forms of respiratory failure,<sup>28</sup> therapy with NPPV lowered intubation and mortality rates in the subgroup of patients with hypoxemic respiratory failure.

These studies indicate that NPPV can improve gas exchange, lower the need for intubation, and reduce mortality rates in patients with hypoxemic respiratory failure.<sup>27,28</sup> However, results have been inconsistent between studies, and the wide variety of patients who fall into this very broad diagnostic category makes it difficult to apply results to individual patients. For this reason, many studies have focused on the efficacy of NPPV in single diagnostic subcategories, and these studies are discussed below.

### Cardiogenic Pulmonary Edema

Cardiogenic pulmonary edema, along with COPD exacerbation, is one of the two most common diagnoses among recipients of noninvasive positive-pressure techniques in the acute setting.<sup>29</sup> The evidence supporting the use of positive-pressure therapy in patients with pulmonary edema, however, is stronger for the use of CPAP than for NPPV (in which air pressure is increased during inspiration). CPAP has been used for many decades to treat cardiogenic pulmonary edema, and the rationale for its application is quite strong. In such patients, CPAP rapidly improves oxygenation by reexpanding flooded alveoli, increasing functional residual capacity, and thereby more favorably positioning the lung on its compliance curve.<sup>30</sup> These effects lead to a reduction in the work of breathing and can improve cardiac performance.<sup>30-32</sup> The latter effect is achieved by raising pericardial pressure, lowering transmural pressure, and thereby decreasing afterload.<sup>33,34</sup> This favorable hemodynamic effect is most likely to occur when filling pressures are high and ventricular performance is poor. However, in patients with relatively low filling pressures and good ventricular performance, the hemodynamic effects of CPAP can be adverse, by diminishing venous return.<sup>31</sup>

A number of studies<sup>35-39</sup> have demonstrated that CPAP is effective in treating patients with acute pulmonary edema (Table 3). Rasanen et al<sup>35</sup> randomized 40 patients with cardiogenic pulmonary edema to either face-mask CPAP (10 cm H<sub>2</sub>O) or standard medical therapy, and demonstrated a rapid improvement in oxygenation and respiratory rate. Lin and Chiang<sup>37</sup> randomized 55 patients to face-mask CPAP that was adjusted, along with FIO<sub>2</sub>, to maintain PaO<sub>2</sub> at  $\geq 80$  mm Hg. CPAP significantly lowered the rate of intubation compared to standard oxygen therapy (17.5% vs 42.5%, respectively;  $p < 0.05$ ), but no significant difference in mortality rate was observed. Bersten et al<sup>38</sup> and Lin et al<sup>39</sup> subsequently performed similar randomized studies on 39 and 100 patients, respectively, demonstrating the same favorable effects on oxygenation, respiratory rates, and the need for intubation. The study by Bersten et al<sup>38</sup> also showed a significant reduction in ICU length of stay among CPAP-treated patients, and the study by Lin et al<sup>39</sup> showed trends for improved hospital mortality rate.

Fewer controlled trials have been performed to determine whether NPPV is effective therapy for patients with acute pulmonary edema. Hypothetically, NPPV might be more effective than CPAP alone, because a greater reduction in the work of breathing and a more rapid alleviation of hypercapnia and dyspnea might be superimposed on the benefits achieved with CPAP.

Several uncontrolled trials support the likelihood that NPPV is an effective therapy for patients with acute pulmonary edema by demonstrating low intubation and complication rates.<sup>17,25,40-42</sup> However, one of these studies<sup>42,43</sup> noted a high mortality rate in patients with acute myocardial infarction and cautioned about the use of NPPV in them. In a randomized, prospective trial of 40 patients who had been treated with mean inspiratory and expiratory pressures of 15 and 5 cm H<sub>2</sub>O, respectively, Masip et al<sup>44</sup> found a significantly lower rate of intubation in NPPV-treated patients (5%) compared to oxygen-treated control subjects (33%;  $p = 0.037$ ). While

**Table 3—Summary of Trials Using CPAP in Acute Pulmonary Edema**

Study/Year	Patients, No.		Failures, No. (%)*		p Value
	NPPV Group	Control Group	NPPV Group	Control Group	
Rasanen et al <sup>35</sup> /1985	20	20	7 (35)	13 (65)	0.068
Viasanen and Rasanen <sup>36</sup> /1987	40		7 (17.5)		NA
Lin and Chiang <sup>37</sup> /1991	25	30	7 (28)	18 (60)	< 0.05
Bersten et al <sup>38</sup> /1991	19	20	0 (0)	7 (35)	< 0.05
Lin et al <sup>39</sup> /1995	50	50	8 (16)	18 (36)	< 0.05

\*Including patients who were intubated or failed to tolerate the mask.

oxygenation improved more rapidly in the NPPV-treated group compared to the control group, hospital lengths of stay and mortality rates were similar in the two groups. Sharon et al<sup>45</sup> also performed a randomized trial that compared NPPV plus low-dose nitroglycerin vs high-dose nitroglycerin in 40 patients with acute pulmonary edema. Patients treated with NPPV had a higher intubation rate (80% vs 20%, respectively), myocardial infarction rate (55% vs 10%, respectively), and death rate (10% vs none, respectively) compared to control subjects (all  $p < 0.05$ ), leading the authors to conclude that NPPV was less effective and was potentially harmful compared to therapy with high-dose nitroglycerin. However, this inference is unjustified because the groups were not comparable and the inordinately high intubation rate in the NPPV group (80%) is difficult to explain.

The superiority of NPPV over the standard therapy for acute pulmonary edema is not surprising, but the question of most interest is whether NPPV is superior to CPAP alone. If not, then the simpler and less expensive CPAP devices could be used to treat patients with acute pulmonary edema. Only one randomized trial<sup>46</sup> has thus far compared CPAP to NPPV in the treatment of patients with acute pulmonary edema. Although this trial showed significantly more rapid reductions in respiratory rate, dyspnea score, and hypercapnia in the NPPV-treated group compared to the CPAP-treated group, the study was stopped prematurely after the enrollment of 27 patients because of a greater myocardial infarction rate in the NPPV group. While this difference may have been attributable to unequal randomization because more patients in the NPPV group presented with chest pain, the results nonetheless raise concerns about the safety of the ventilatory techniques used to treat acute pulmonary edema complicated by cardiac ischemia or infarction. A more recent randomized controlled trial<sup>47</sup> compared NPPV to high-flow oxygen by mask and demonstrated no statistically significant difference in the myocardial infarction rate between the two groups. However, this study had limitations, including its small size and the probable use of inadequate pressures, considering that respiratory rate was not lowered more by NPPV. Pending further studies, the most sensible recommendation is to use CPAP (10 cm H<sub>2</sub>O) initially and to consider switching to NPPV if the patient is found to have substantial hypercapnia or unrelenting dyspnea. This recommendation is in line with the conclusion of a meta-analysis<sup>48</sup> that found insufficient evidence to support the use of NPPV in preference to CPAP to treat patients with acute pulmonary edema.

## Pneumonia

*Severe Community-Acquired Pneumonia:* The application of NPPV to the treatment of patients with acute pneumonia has generated conflicting reports. Early on, pneumonia was associated with a poor outcome in patients treated with NPPV.<sup>49</sup> Subsequently, a randomized trial<sup>50</sup> of 56 patients found that NPPV reduced the need for intubation (21% vs 50%, respectively;  $p = 0.03$ ), shortened ICU length of stay (1.8 vs 6 days, respectively;  $p = 0.04$ ), and reduced mortality rate among the COPD subgroup of patients 2 months after hospital discharge. However, further analysis showed that the COPD subgroup was the only one to benefit from NPPV. More recently,<sup>51</sup> a prospective trial focusing on NPPV use in non-COPD patients with severe community-acquired pneumonia observed that 22 of 24 patients had initial improvements in oxygenation and respiratory rates after starting NPPV, but that 66% of patients eventually required intubation. Although the authors concluded that a trial of NPPV should be routine in patients with community-acquired pneumonia, the lack of control subjects undermines this conclusion. Based on the above evidence, the initiation of NPPV therapy is warranted in appropriate COPD patients with pneumonia, but the benefit of NPPV therapy in pneumonia patients without COPD has not been established. As such, NPPV therapy should be used with caution in such patients.

*Immunocompromised Patients:* Evidence is accumulating to support the use of NPPV in immunocompromised patients with acute respiratory failure. Among 40 patients who developed acute respiratory failure following solid organ transplant, those randomized to receive NPPV more often had increases in PaO<sub>2</sub>/FIO<sub>2</sub> ratios (60% vs 25%, respectively;  $p = 0.03$ ), lower intubation rates (20% vs 70%, respectively;  $p = 0.05$ ), and lower mortality rates (20% vs 50%, respectively;  $p = 0.05$ ) than conventionally treated control subjects.<sup>52</sup> In addition, the incidence of severe sepsis and shock was significantly reduced in the NPPV group. More recently, another randomized trial<sup>53</sup> of 52 patients with various immunocompromised states, mainly related to hematologic malignancy, demonstrated reductions in the need for intubation (46% vs 76%, respectively;  $p = 0.03$ ) and serious complication and mortality rates (both 50% vs 80%, respectively;  $p = 0.02$ ) in NPPV-treated patients compared with conventionally treated control subjects. Although the mortality rate remained high among NPPV-treated patients in the latter study, the mortality rate of patients with hematologic malignancies who required intubation has been reported to be  $> 80\%$  in some series,<sup>54-60</sup>

largely because of septic and hemorrhagic complications. Thus, the avoidance of intubation in this patient population is a desirable outcome, and the use of NPPV is, therefore, justifiable in selected patients with immunocompromised states. It is important to note, however, that the authors of these studies stress the importance of early initiation of therapy before progression to severe compromise.<sup>53</sup>

### ARDS

The use of NPPV has been reported to maintain adequate oxygenation and avert intubation in 6 of 12 episodes of ARDS in 10 patients.<sup>61</sup> However, no controlled trials have been performed to assess the effect of NPPV on morbidity or mortality rates in ARDS patients, and, thus, its use in such a patient group is rarely justified. While NPPV can be tried in patients with early, relatively mild ARDS in an attempt to avoid intubation, routine use is not advised, particularly in patients with multiorgan system failure who are likely to require prolonged ventilatory support using sophisticated ventilator modes. If a trial of NPPV is initiated, patients should be closely monitored and promptly intubated if their conditions deteriorate, so that inordinate delays in needed interventions are avoided.

### Trauma

Trauma patients develop respiratory failure for a multitude of reasons, but some have chest wall injuries such as flail chest or mild acute lung injury that might respond favorably to NPPV therapy. In a retrospective survey of 46 trauma patients with respiratory insufficiency that had been treated with NPPV, Beltrame et al<sup>62</sup> found rapid improvements in gas exchange and a 72% success rate; however, those patients with burns responded poorly. Despite these promising results, the uncontrolled design of the study limits the ability to draw conclusions or to make recommendations on the use of NPPV in trauma patients.

### RESTRICTIVE DISEASES

NPPV is considered to be the ventilatory modality of first choice to treat chronic respiratory failure in patients with thoracic restriction caused by neuromuscular disease or chest wall deformity.<sup>63</sup> However, few studies have examined the use of NPPV when these patients become acutely ill, partly because they constitute a very small portion of the patients with respiratory failure entering acute care hospitals.<sup>17</sup> Some retrospective series have suggested that NPPV alleviates gas exchange abnormalities and

avoids intubation in patients with neuromuscular disease<sup>64</sup> and kyphoscoliosis<sup>65</sup> who are experiencing acute respiratory failure. For managing acute deteriorations in patients already using NPPV at home for chronic respiratory failure due to neuromuscular disease, Bach et al<sup>66</sup> have recommended increasing the duration of use to 24 h per day while continuously monitoring pulse oximetry. If O<sub>2</sub> saturation falls to < 90%, aggressive removal of secretions is undertaken using manually assisted coughing and mechanical aids, such as the cough insufflator-exsufflator,<sup>66</sup> until oxygen saturation returns to > 90%. No controlled studies have established the efficacy of this approach, but the data from the study by Bach et al<sup>66</sup> have suggested that its use during acute exacerbations dramatically reduces the need for hospitalization.

Although mentioned in case series,<sup>17</sup> little information is available on the use of NPPV to treat acutely deteriorating patients with restrictive lung diseases such as interstitial fibrosis. Considering that severe hypoxemia and low lung compliance characterize the terminal stages of these diseases, NPPV would not be expected to offer much benefit, unless an acutely reversible superimposed condition was thought to be responsible for the deterioration.

### POSTOPERATIVE PATIENTS

Some early case series reported the use of NPPV in the treatment of respiratory insufficiency after surgery in patients with PaCO<sub>2</sub> levels of > 50 mm Hg, PaO<sub>2</sub> values of < 60 mm Hg, or evidence of respiratory muscle fatigue.<sup>67-70</sup> Using nasal bilevel pressure ventilation, these studies reported prompt reductions in respiratory rate and dyspnea scores, improvements in gas exchange, and high success rates in avoiding the need for reintubation. Subsequently, prophylactic postoperative use of NPPV in lung resection patients<sup>71</sup> and postgastroplasty patients<sup>72</sup> has been shown to improve gas exchange and pulmonary function, respectively, compared to control subjects who were treated with oxygen alone. More recently, a randomized trial of NPPV in post-lung resection patients with acute respiratory insufficiency showed significant reductions in the need for intubation, ICU length of stay, and mortality rate compared to conventionally treated control subjects.<sup>73</sup> Thus, accumulating evidence now supports the use of NPPV in selected postoperative patients to maintain improved gas exchange and to avoid reintubation and its attendant complications. It should be noted, however, that NPPV is considered to be contraindicated after upper airway or esophageal surgery, and many surgeons have concerns about its

application after gastric or small intestinal surgery that has disrupted bowel wall integrity.

#### DO-NOT-INTUBATE PATIENTS

The use of NPPV to treat respiratory failure in patients who have declined intubation is common in some centers, accounting for some 10% of short-term applications in one survey.<sup>74</sup> Some have argued<sup>75</sup> that there is little to lose with this approach, as it may reverse the acute deterioration or, at least, afford relief from dyspnea and a few extra hours to finalize the patient's affairs. However, others have argued that this merely prolongs the dying process, consumes resources inappropriately, and may add to discomfort or be counter to patients' wishes about the avoidance of life-prolonging measures.<sup>76</sup> In one study<sup>77</sup> of 30 patients, mostly those with COPD, in whom endotracheal intubation was "contraindicated or postponed," 18 patients (60%) were successfully supported with NPPV and weaned. Another uncontrolled series<sup>78</sup> observed a similar response to NPPV among 26 patients with acute hypercapnic and hypoxemic respiratory failure who had refused intubation. In a more recent prospective survey<sup>74</sup> of 113 do-not-intubate (DNI) patients who had been treated with NPPV, the survival rate to hospital discharge was 72% and 52%, respectively, for acute pulmonary edema and COPD patients, whereas it was < 25% for those who had received diagnoses of pneumonia or cancer. Thus, the use of NPPV may be justifiable in DNI patients with acutely reversible processes such as acute pulmonary edema or COPD exacerbation. If used in such instances, however, patients and/or their families should be informed that NPPV is being used as a form of life support that may be uncomfortable and can be removed at any time.

#### FACILITATION OF EXTUBATION AND WEANING

NPPV has been used to facilitate early extubation after bouts of acute respiratory failure and to avoid extubation failure when the condition of a patient deteriorates following extubation. In the first instance, NPPV is used after extubation in patients who fail to meet standard extubation criteria, based on the presumption that outcomes can be improved by avoiding the complications of prolonged intubation such as nosocomial infection and upper airway trauma. The first controlled trial<sup>79</sup> to test this idea enrolled 50 COPD patients who had been intubated for 48 h and had failed a T-piece trial. Twenty-five patients were randomized to NPPV after early extu-

bation, and the remaining 25 patients remained intubated and were weaned gradually using pressure support and daily spontaneous breathing trials. Patients randomized to receive NPPV had higher overall weaning rates after 60 days (88% vs 68%, respectively), shorter durations of mechanical ventilation (10.2 vs 16.6 days, respectively), briefer stays in the ICU (15.1 vs 24 days, respectively), and improved 60-day survival rates (92% vs 72%, respectively) compared to control subjects (all  $p < 0.05$ ). In addition, among NPPV-treated patients there were no cases of nosocomial pneumonia compared to seven cases among those in the control group.

A second randomized, controlled trial<sup>80</sup> of 33 patients with acute-on-chronic respiratory failure addressed the question of whether NPPV should be used as a "systematic" extubation technique. Patients randomized to early extubation and NPPV had shorter durations of invasive mechanical ventilation than did those in the intubated control group (4.56 vs 7.69 days, respectively;  $p < 0.05$ ), but the total duration of mechanical ventilation (including NPPV) was actually greater in the NPPV group (16.1 vs 7.69 days, respectively;  $p = 0.0001$ ). Furthermore, patients in the NPPV group had similar eventual weaning and mortality rates, and, although they had a tendency toward fewer complications (16% vs 9%, respectively), the difference was not statistically significant. The authors concluded that NPPV shortens the duration of invasive mechanical ventilation, but they were unable to demonstrate significant improvements in other outcomes. A third controlled, preliminary trial of 25 patients with various etiologies for their acute respiratory failure also found a significantly shorter duration of invasive mechanical ventilation, but the extubation failure rate was higher (41% vs none in control subjects;  $p < 0.05$ ) among patients extubated early to NPPV.<sup>81</sup>

These studies present a mixed picture regarding the routine use of NPPV to shorten the duration of invasive mechanical ventilation. Clinicians are advised to exert caution when selecting patients for early extubation, reserving the technique mainly for patients with acute-on-chronic respiratory failure who are unable to meet standard extubation criteria but are otherwise good candidates for noninvasive ventilation.

NPPV can also potentially be used to avoid reintubation in patients who fail extubation. Extubation failure occurs after 5 to 20% of planned extubations<sup>82</sup> and after 40 to 50% of unplanned extubations,<sup>83</sup> and has been associated with a mortality rate of 43% compared to only 12% in those patients who succeed after extubation.<sup>82</sup> Several studies<sup>17,84-87</sup> have examined the idea that NPPV can be used to avert the need for reintubation in patients with

extubation failure, thereby avoiding the complications and mortality of prolonged intubation. Another study<sup>86</sup> found that 30 COPD patients with postextubation hypercapnic respiratory insufficiency who had been treated with NPPV required reintubation less often (20% vs 67%, respectively;  $p < 0.05$ ) and had shorter ICU lengths of stay than did 30 historically matched control subjects.

To date, the only randomized trials that have been published examined NPPV as a "prophylactic" technique, using it in all extubated patients to see whether the extubation failure rate could be lowered.<sup>87,88</sup> Jiang et al<sup>87</sup> enrolled 93 consecutive patients, 56 after planned extubations and 37 after unplanned extubations. Thirteen of the 47 patients (28%) randomized to NPPV required reintubation compared to only 7 of the 46 control subjects (15%) who had received therapy with O<sub>2</sub> supplementation alone ( $p > 0.05$ ). Although there was a problem with randomization in that more patients with unplanned extubations were assigned to the NPPV group, and these patients constituted most of the failures, the authors concluded that their results did not support the "indiscriminate" use of NPPV to avoid postextubation failure. Keenan et al<sup>88</sup> evaluated 81 patients who were initially intubated for various cardiac and respiratory diseases for at least 2 days and developed respiratory distress within 48 h of extubation. Patients were randomized in an unblinded manner to receive standard medical therapy alone<sup>42</sup> or NPPV by face mask plus standard medical therapy.<sup>39</sup> The rate of reintubation was similar in both groups (control group, 69%; NPPV group, 72%;  $p = 0.79$ ), but there were three patients who were randomized to NPPV but received standard therapy. The authors commented that in an analysis for selection bias they identified 44 patients who fulfilled the inclusion criteria and had received NPPV outside the study, and that among these patients there was a trend toward lower reintubation rate ( $p = 0.08$ ). Thus, the evidence to support the use of NPPV to avoid reintubation in patients with extubation failure appears inconclusive and is perhaps confounded by the problem of selection bias. Despite the lack of adequate controlled trials to support its use in this setting, however, this application is justifiable as long as patients are selected carefully and are closely monitored until stabilized.

#### PATIENT SELECTION

The success of NPPV is partly related to the skill of the medical team in selecting appropriate patients. The selection process takes into consideration a number of factors, including the patient's diagnosis,

clinical characteristics, and risk of failure, and ultimately becomes a clinical judgment that depends largely on physician experience. The etiology and reversibility of the respiratory failure are key, and clinicians should consider the evidence supporting the use of NPPV for a particular diagnosis, as discussed above.

Predictors of the success of NPPV have been identified by some studies<sup>49,84,89,90</sup> and are outlined in Table 4. As might be anticipated, these studies have shown that patients with a better neurologic status (and hence are more cooperative) who are able to adequately protect their airway and have not developed severe acid-base or gas exchange derangements are more likely to succeed. Several studies<sup>89-91</sup> also have found that a patient's initial response to NPPV after 1 h of treatment (demonstrated by improvements in pH, PaCO<sub>2</sub>, and level of consciousness) are associated with success. These studies<sup>49, 84, 89-91</sup> also indicate that there is a "window of opportunity" when initiating NPPV. The window opens when patients become distressed enough to warrant ventilatory assistance but closes if they progress too far and become severely acidemic. Thus, the early initiation of NPPV is recommended so that patients have time to adapt and respiratory crises can be averted. Contrary to this, therapy with NPPV that is begun too early might be unhelpful and wasteful of resources because many treated patients might do well without any ventilatory assistance. For this reason, selection guidelines have recommended first establishing the need for ventilatory assistance, according to clinical and blood gas criteria, and then excluding patients in whom NPPV is contraindicated or who are likely to fail (Table 5).

**Table 4—Determinants of Success for NPPV in the Acute Setting**

Synchronous breathing <sup>89</sup>
Dentition intact <sup>89</sup>
Lower APACHE score <sup>49,89</sup>
Less air leaking <sup>89</sup>
Less secretions <sup>89</sup>
Good initial response to NPPV <sup>49,89,91</sup>
Correction of pH <sup>91</sup>
Reduction in respiratory rate
Reduction in PaCO <sub>2</sub> <sup>91</sup>
No pneumonia <sup>89,49</sup>
pH > 7.10 <sup>49</sup>
PaCO <sub>2</sub> < 92 mm Hg <sup>49</sup>
Better neurologic score <sup>49,91</sup>
Better compliance* <sup>49</sup>

\*Compliance<sup>49</sup> or tolerance<sup>91</sup> refers to the clinician's assessment of the patient's acceptance of the technique.

**Table 5—Selection Criteria for NPPV in the Acute Setting**

Appropriate diagnosis with potential reversibility
Establish need for ventilatory assistance
Moderate to severe respiratory distress
Tachypnea
Accessory muscle use or abdominal paradox
Blood gas derangement
pH < 7.35, PaCO <sub>2</sub> > 45 mm Hg, or
PaO <sub>2</sub> /FIO <sub>2</sub> < 200
Exclude patients with contraindications to NPPV
Respiratory arrest
Medically unstable
Unable to protect airway
Excessive secretions
Uncooperative or agitated
Unable to fit mask
Recent upper airway or gastrointestinal surgery

**BASIC CONSIDERATIONS FOR INITIATION OF NPPV**

In addition to proper patient selection, the successful implementation of NPPV requires the use of a comfortable interface (or mask), the optimal setting of the ventilator, appropriate monitoring, and, most of all, the conscientious attention of a skilled health-care team.

**Mask Selection**

The masks most commonly chosen for short-term applications of NPPV are commercially available oronasal (full-face) masks or nasal masks. Important considerations when choosing between masks are listed in Table 6. In the United States, these are most commonly inexpensive disposable varieties of masks

**Table 6—Nasal vs Oronasal (Full-Face) Masks: Advantages and Disadvantages\***

Variables	Nasal	Oronasal
Comfort	+++	++
Claustrophobia	+	++
Rebreathing	+	++
Lowers CO <sub>2</sub>	+	++
Permits expectoration†	++	+
Permits speech‡	++	+
Permits eating§	+	-
Functions if nose obstructed	-	+

\*+ = possible; ++ = more likely; +++ = most likely; - = not possible.

†Expectoration is possible but requires the assistance of a respiratory therapist with the oronasal mask.

‡Speech is possible but may vary depending on the degree of respiratory failure.

§Eating necessitates oronasal mask removal and may be contraindicated in patients with severe respiratory failure.

that have soft silicone seals. Controlled studies that have compared masks are few, but one recent study<sup>92</sup> randomized 70 patients with acute respiratory insufficiency to receive a nasal or oronasal mask. Both masks performed similarly with regard to improvements in vital signs and gas exchange, and the avoidance of intubation, but the nasal mask was initially less well-tolerated, mainly because of excessive mouth leaks.<sup>92</sup> In a second controlled trial<sup>93</sup> in patients with chronic respiratory failure, the oronasal mask lowered CO<sub>2</sub> more effectively than the nasal mask or prongs, but the nasal mask was sensed as more comfortable. Thus, a sensible approach is to start with an oronasal mask for most short-term applications and to switch to a nasal mask if prolonged use (*ie*, > 2 to 3 days) is contemplated. Whichever mask is chosen, a comfortable fit is of paramount importance, and care must be taken to use the minimum strap tension that achieves an adequate air seal so that pressure sores are avoided.

**Ventilator Selection**

Ventilator selection is probably not as important as that of mask selection because most ventilators can be adjusted to deliver NPPV. Until recently, the choice has been between critical care ventilators, which were designed for invasive mechanical ventilation, and bilevel devices, which were first designed for therapy for sleep apnea but proved to be effective pressure-limited ventilators.<sup>8</sup> Neither type is ideal, and both have advantages and disadvantages (Table 7). Either type can be used successfully for most short-term applications, although ventilators with oxygen blenders are preferred for patients with hypoxemic respiratory failure. On the other hand, the bilevel devices, because they were designed to deliver NPPV, are more leak-tolerant and less likely to sound alarms inappropriately than are critical care ventilators. Bilevel ventilators also promote rebreathing by virtue of their

**Table 7—Critical Care vs Bilevel Ventilators\***

Variables	Ventilators	
	Critical Care	Bilevel†
Inspiratory pressure	++	++
Leak tolerant	+	++
Different modes	++	+
Alarms	++	+
Monitoring capability	++	+
Battery	-	-
Oxygen blender	++	-
Compactness	+	++

\*+ = present; ++ = better; - = absent.

†Newer bilevel devices incorporate graphic monitors, oxygen blenders, and sophisticated alarms for use in the acute setting.

single inspiratory and expiratory tubing, but this can be minimized by assuring adequate expiratory bias flow (with adequate expiratory pressure and a suitable expiratory port).<sup>94,95</sup> Recently, a number of ventilator manufacturers have introduced ventilators that were designed to deliver either invasive or noninvasive ventilation. These have more sophisticated alarm and monitoring capabilities than the traditional bilevel devices. When in the noninvasive mode, they are leak-tolerant and use only the alarms essential for the operation of NPPV, silencing other alarms that are not needed.

### Ventilator Settings

Pressure-limited modes are preferred for most short-term applications because they are sensed as more comfortable than volume-limited modes.<sup>96,97</sup> Patient-ventilator asynchrony may contribute to failure, and using a mode that permits the limitation of maximal inspiratory time (such as pressure-control or newer bilevel modes) may improve synchrony, particularly in the presence of leaks.<sup>98</sup> Newer modes such as proportional assist ventilation may offer some advantages such as greater comfort and ease of initiation over traditional pressure-support modes,<sup>99</sup> but this is not yet available in the United States.

Inspiratory pressure may be set by starting relatively low (*ie*, 8 to 10 cm H<sub>2</sub>O) and gradually increasing as tolerated,<sup>8</sup> or by starting high (*ie*, 15 to 20 cm H<sub>2</sub>O) and gradually working down if the patient is intolerant.<sup>17</sup> Inspiratory pressures of > 20 cm H<sub>2</sub>O are discouraged in order to minimize adverse side effects such as sinus pain and gastric insufflation. The authors favor starting with low pressures as a better way to avoid intolerance caused by excessive pressure. In essence, the clinician is attempting to unload the breathing muscles and alleviate respiratory distress while avoiding the excessive discomfort caused by air pressure and flow. Inspiratory pressure can only be optimized by a trial-and-error titration process performed at the bedside over a period of time.

Expiratory pressure is most often set at 4 to 5 cm H<sub>2</sub>O to assure adequate bias flow with bilevel devices and counterbalance auto-positive end-expiratory pressure in COPD patients. Higher pressures are not often needed but might be tried in patients with diffuse parenchymal involvement and persisting hypoxemia, or to minimize apneas and hypopneas in patients with obstructive sleep apnea. When adjusting expiratory pressure, the inspiratory pressure must be adjusted in parallel if the level of pressure support is to remain constant.

### Adjuncts to Ventilation

With the exception of some newer devices, most bilevel ventilators lack oxygen blenders. Oxygen is supplemented by attaching tubing to a nipple on the mask or to a T-connector inserted in the ventilator tubing. The oxygen flow rate then is adjusted to keep O<sub>2</sub> saturation above a certain level, usually 90 to 92%. Because of gas mixing and leaking, FIO<sub>2</sub> values of > 45 to 50% are difficult to achieve with bilevel devices, even using maximal flow rates of 15 L/min. Also, higher oxygen flow rates usually are required to achieve a given oxygen saturation target with NPPV than with nasal prongs alone. Thus, patients with severe oxygen defects are better managed using ventilators with oxygen blenders that are capable of delivering high levels of FIO<sub>2</sub>.

Few studies have examined the effect of humidification on NPPV tolerance or outcomes, but it appears to add to patient comfort and ease of expectoration, and is recommended by the authors if NPPV use is expected to exceed 8 to 12 h or if the patient has thick secretions. Unless clearly indicated, the routine use of a gastric tube for oronasal masks is not recommended because they interfere with maintenance of a tight air seal.

### COMPLICATIONS OF NPPV

The complications of NPPV are usually minor. The most frequently encountered adverse effects are related to the mask and ventilator airflow pressure.<sup>100</sup> Accounting for a large portion of the reported complications are nasal bridge or mucosal pain, or nasal bridge erythema or ulceration.<sup>101,102</sup> These complications can be minimized or avoided by minimizing strap tension, using forehead spacers, or routinely applying artificial skin to the area.<sup>100</sup> Other less common but noteworthy complications that are encountered include claustrophobia, nasal congestion, sinus/ear pain, mucosal dryness, eye irritation, and gastric insufflation.<sup>100</sup> Rarely (*ie*, < 5%) is NPPV associated with major complications such as hypotension, aspiration, and pneumothorax.<sup>8,100</sup> Understanding and recognizing the potential adverse complications of NPPV are imperative so that interventions can be initiated or NPPV discontinued in the appropriate setting.

### UTILIZATION OF NPPV IN ACUTE SETTINGS

A survey of utilization at a university hospital in Canada found that therapy with NPPV was most often begun in the emergency department and that acute pulmonary edema and exacerbation of COPD

were the most common indications in 44% and 24% of applications, respectively.<sup>103</sup> NPPV therapy was used for a median of only 4.9 h, and the intubation rate was 25.6%. Bilevel ventilation was most often prescribed, at median inspiratory and expiratory pressures of 10 and 5 cm H<sub>2</sub>O, respectively. The authors noted that the intubation rate was higher than in most prior randomized controlled trials, raising the concern that the inspiratory pressure may have been too low to achieve the optimal therapeutic effect, and suggested that practice guidelines would be useful in optimizing outcomes. In a second survey<sup>29</sup> that was conducted in 42 ICUs in Europe, NPPV was used in 48% of patients with hypercapnic respiratory failure and in 35% of all patients who received mechanical ventilation after entering the ICU. However, utilization varied substantially between institutions, ranging from 0% in eight ICUs to 67% in one ICU.<sup>29</sup> The finding that NPPV usage varies so much indicates that the modality is underutilized at some centers. Possible explanations for this include reluctance on the part of physicians, nurses, or therapists to use the modality, inadequate training or staffing, or lack of appropriate equipment. In order to offer optimal therapy to patients with types of respiratory failure that have been shown to respond favorably to NPPV, centers not using NPPV are encouraged to seek training and experience in using the modality. The overutilization of NPPV is also a concern, particularly if its inappropriate application leads to the delay of needed intubations and the squandering of resources.

#### PERSONNEL TIME CONSUMPTION AND FINANCIAL CONSIDERATIONS

An early analysis<sup>104</sup> that raised concerns about the excessive time consumption associated with using NPPV found that a nurse was at the bedside 91% of the time that NPPV was being administered to patients with COPD exacerbations. However, subsequent analyses have not borne this concern out. In one randomized trial,<sup>8</sup> respiratory therapists spent an average of approximately 1 h more treating NPPV patients during the first 8-h shift compared to conventionally treated control subjects, although the difference was not statistically significant. Time consumption by therapists fell significantly by the second shift, and time consumption by nurses was similar throughout. A second nonrandomized trial<sup>105</sup> found that although therapists spent significantly more time administering NPPV than invasive mechanical ventilation during the first 6 h, there were no significant differences at 48 h. Furthermore, there were no significant differences for the time expenditure of nurses or physicians. Therefore, it ap-

pears that NPPV requires slightly more time for initiation than invasive mechanical ventilation, usually from the respiratory therapist.

The cost of administering NPPV also has been examined in several studies.<sup>8,105-108</sup> In an earlier randomized trial,<sup>8</sup> hospital charges were similar between a group treated with NPPV and another receiving conventional treatment. A subsequent nonrandomized trial<sup>105</sup> found similar total costs for NPPV and invasive mechanical ventilation for the first 48 h of therapy for COPD patients. A more recent cost-effectiveness analysis of NPPV compared to invasive mechanical ventilation to treat COPD exacerbations found an average savings of \$3,244 (in 1996 Canadian dollars) per patient hospital admission.<sup>107</sup> Unfortunately, the diagnosis-related group payment system in the United States does not reimburse hospitals adequately for patients treated with NPPV, because it does not qualify for the ventilator code (*International Classification of Diseases*, ninth revision, code 475). As of 1995, this resulted in a \$9,701 (in US dollars) underreimbursement per patient hospital admission when NPPV was used compared to invasive mechanical ventilation.<sup>108</sup> Thus, even though evidence is accumulating indicating that NPPV not only improves outcomes but is also more cost-effective than invasive mechanical ventilation for certain forms of respiratory failure, the diagnosis-related group system fails to reward hospitals for using it.

#### CONCLUSION

NPPV constitutes a therapeutic advance for certain forms of respiratory failure. Current evidence supports the use of NPPV to reduce the need for intubation and its attendant morbidity and mortality in selected patients with respiratory failure caused by COPD exacerbations or pneumonias in patients with COPD or immunocompromised states. Although NPPV is commonly used to treat acute pulmonary edema, the evidence supports the use of CPAP alone for this entity. Evidence is accumulating to support the use of NPPV for other short-term applications, such as postoperative respiratory failure, as a means of facilitating weaning from invasive ventilation or preventing extubation failure, and in some DNI patients. NPPV has been used to treat numerous other causes of acute respiratory failure, but controlled studies to support these applications are lacking (Table 1).

Patient recipients of NPPV should be selected with care using currently available guidelines, and implementation should take place in an appropriately monitored setting, usually an emergency department with transfer to an ICU or stepdown unit

until the patient stabilizes. NPPV administered to appropriate patients by an experienced team using state-of-the art technology improves patient outcomes in a cost-effective manner. Centers not currently using NPPV are encouraged to gain training and experience with the modality, and insurers are encouraged to recognize the value of NPPV and to reimburse health-care providers appropriately.

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