

# Non-invasive ventilation in acute respiratory failure

Stefano Nava, Nicholas Hill

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Respiratory Intensive Care Unit, Fondazione S Maugeri Istituto Scientifico di Pavia, IRCCS, Pavia, Italy (S Nava MD); and Tufts Medical Center, Pulmonary, Critical Care and Sleep Medicine, Boston, MA, USA (N S Hill MD)

Correspondence to: S Nava, Respiratory Intensive Care Unit, Fondazione S Maugeri, Istituto Scientifico di Pavia, Via Maugeri, Pavia 27100, Italy [stefano.nava@fsm.it](mailto:stefano.nava@fsm.it)

Non-invasive mechanical ventilation has been increasingly used to avoid or serve as an alternative to intubation. Compared with medical therapy, and in some instances with invasive mechanical ventilation, it improves survival and reduces complications in selected patients with acute respiratory failure. The main indications are exacerbation of chronic obstructive pulmonary disease, cardiogenic pulmonary oedema, pulmonary infiltrates in immunocompromised patients, and weaning of previously intubated stable patients with chronic obstructive pulmonary disease. Furthermore, this technique can be used in postoperative patients or those with neurological diseases, to palliate symptoms in terminally ill patients, or to help with bronchoscopy; however further studies are needed in these situations before it can be regarded as first-line treatment. Non-invasive ventilation implemented as an alternative to intubation should be provided in an intensive care or high-dependency unit. When used to prevent intubation in otherwise stable patients it can be safely administered in an adequately staffed and monitored ward.

## Introduction

In the late 1980s, when innovators first began using non-invasive ventilation in patients with acute respiratory failure as a potential alternative to endotracheal intubation,<sup>1</sup> few clinicians would have thought that within 20 years this technique would become a first-line intervention for some forms of acute respiratory failure.<sup>2</sup> Non-invasive ventilation refers to the delivery of mechanical ventilation with techniques that do not need an invasive endotracheal airway. It should not, therefore, be used when patients cannot protect their airway. It is not appropriate for all, and the selection of candidates is important (panel 1). For patients with secretion accumulation or a weak cough reflex, adequate secretion management with manual or mechanical techniques might be advisable before non-invasive ventilation is declared failed or contraindicated.<sup>2,3</sup> Compared with invasive mechanical ventilation, this type of ventilation achieves the same physiological benefits of reduced work of breathing and improved gas exchange.<sup>4</sup> Furthermore, it avoids the complications of intubation and the increased risks of ventilator-associated pneumonia and sinusitis, especially in patients who are immunosuppressed or with comorbidities.<sup>2</sup>

We review present and potential uses of non-invasive ventilation in the acute setting, with emphasis on indications outside the intensive care unit. Although continuous positive airways pressure (CPAP) does not actively assist inspiration as do all other forms of non-invasive positive-pressure ventilation, we class CPAP as a non-invasive mode unless otherwise specified.

## Search strategy and selection criteria

We searched Medline, EmBase, and the Cochrane database, using the keywords “non-invasive” or “noninvasive (mechanical) ventilation”, for all reports of adults, published until March, 2009. Our search was not limited to publications in English. We selected relevant reports and comprehensive reviews. We also searched the reference lists of identified publications, selecting relevant articles with an emphasis on research of acute respiratory failure.

The use of non-invasive ventilation varies greatly between hospitals and geographical regions, and has changed over time. Investigators of a worldwide prospective survey of mechanical ventilation noted that use rose from 4% of all ventilators started in 2001, to 11% in 2004.<sup>5</sup> It is increasingly being used in many countries, but frequency of use is highly variable.<sup>6,7</sup> Non-invasive ventilation is used mainly for exacerbations of chronic obstructive pulmonary disease (COPD) and for cardiogenic pulmonary oedema. Use for hypoxic respiratory failure and facilitation of weaning is still infrequent and is mainly done in specialised centres.<sup>7</sup>

In Europe, the rate of use of non-invasive ventilation in intensive care units is about 35% of ventilated patients and higher (roughly 60%) in respiratory intensive care units or emergency departments.<sup>8,9</sup> In North America, this form of ventilation is begun most often in emergency departments, with most patients transferred to intensive care units or step-down units in hospitals that have such facilities. The low rate of use in some hospitals relates to little knowledge about or experience with the technique, insufficient technical equipment, and inadequate funding.<sup>9–11</sup> Despite these limitations, this technique is increasingly being used outside the traditional and respiratory intensive care units, including in emergency departments; postsurgical recovery rooms;<sup>12</sup> cardiology,<sup>13</sup> neurology,<sup>14</sup> and oncology<sup>15</sup> wards; and palliative care units.<sup>16</sup>

## Use outside intensive care units

In a matched case-control study, Girou and colleagues<sup>17</sup> showed that compared with endotracheal intubation non-invasive ventilation was associated with a lower risk of nosocomial infections (including urinary tract and catheter-related infections), less antibiotic use, shorter lengths of stay in the intensive care units, and lower mortality than was endotracheal intubation. Furthermore, endotracheal intubation is uncomfortable for patients and increases the need for sedation and analgesia, which is an independent factor for extended weaning.<sup>18</sup> During non-invasive ventilation, the need for sedation is usually less than with intubation so that patients maintain better spontaneous breathing, can wean more rapidly, and

spend less time in the intensive care units.<sup>19</sup> However, it should not be used in patients with contraindications (panel 1). Such patients need prompt intubation and inadvisable use places them at risk of need for emergency intubation with its attendant morbidity and mortality.<sup>20</sup>

Non-invasive ventilation can be used in a wide range of disorders that lead to acute respiratory failure. We examine the evidence lending support to applications which are graded according to the Oxford Centre for Evidence-based Medicine (panel 2).<sup>21</sup> The success of this technique depends not only on the diagnosis of respiratory failure and patients' characteristics but also on when the ventilation is started<sup>22</sup> and the setting in which the patient is treated.<sup>23</sup>

Early use of non-invasive ventilation is recommended because the opportunity for a successful start might be lost if delays arise and the patient's underlying disease progresses too far. However, such ventilation can be started too early—ie, when the patient's illness is so mild that no ventilatory assistance is needed and they are more likely to be intolerant than be helped.<sup>24</sup> Thus judgment should be exercised; most practitioners seek evidence of increased dyspnoea and work of breathing (tachypnoea or heightened accessory muscle use).<sup>25</sup> Another advantage of an early start is that patients who are not in immediate life-threatening situations can be managed outside the intensive care units, provided that the ward team has the necessary skills. Hence specialised units (ie, respiratory intensive care, high-dependency) are ideal for provision of non-invasive ventilation to all but the most sick patients because they offer complete non-invasive monitoring systems and higher nurse to patient ratios than are available on general wards.

Patients with acute respiratory acidosis caused by an exacerbation of COPD are the group that benefits most from non-invasive ventilation. Early use in patients with COPD who have with mild respiratory acidosis (as low as pH 7.30) and mild-to-moderate respiratory distress prevents further deterioration, and thus avoids endotracheal intubation and improves survival compared with standard medical therapy.<sup>26</sup> In a large multicentre trial in patients with mild-to-moderate acidotic COPD who were admitted to a respiratory ward, Plant and colleagues<sup>26</sup> noted that intubation and mortality rates were lower with non-invasive ventilation than with standard therapy alone, but subgroup analysis showed that these rates did not differ when pH at enrolment was less than 7.30. The investigators surmised that these patients with low pHs might have fared better in an intensive care unit than in the respiratory ward.

Strong evidence of efficacy (from randomised controlled trials and meta-analyses) and low risk of failure (10–20%) means that use of non-invasive ventilation to avoid intubation in patients with mild-to-moderate COPD and acute respiratory failure (pH 7.30–7.34) is regarded as the ventilatory therapy of first choice and can be safely administered in appropriately monitored and staffed

### Panel 1: Indications and contraindications for NIV in acute care

#### Indications

##### Bedside observations

- Increased dyspnoea—moderate to severe
- Tachypnoea (>24 breaths per min in obstructive, >30 per min in restrictive)
- Signs of increased work of breathing, accessory muscle use, and abdominal paradox

##### Gas exchange

- Acute or acute on chronic ventilatory failure (best indication), PaCO<sub>2</sub>>45 mm Hg, pH<7.35
- Hypoxaemia (use with caution), PaO<sub>2</sub>/F<sub>i</sub>O<sub>2</sub> ratio<200

#### Contraindications

##### Absolute

- Respiratory arrest
- Unable to fit mask

##### Relative

- Medically unstable—hypotensive shock, uncontrolled cardiac ischaemia or arrhythmia, uncontrolled copious upper gastrointestinal bleeding
- Agitated, uncooperative
- Unable to protect airway
- Swallowing impairment
- Excessive secretions not managed by secretion clearance techniques
- Multiple (ie, two or more) organ failure
- Recent upper airway or upper gastrointestinal surgery

NIV=non-invasive ventilation; PaCO<sub>2</sub>=arterial partial pressure of carbon dioxide; PaO<sub>2</sub>=arterial partial pressure of oxygen; F<sub>i</sub>O<sub>2</sub>=fraction of inspired oxygen.

areas outside intensive care.<sup>27–29</sup> Patients with a low pH are still candidates for this technique but transfer to a closely monitored location is strongly advisable.

Non-invasive ventilation has been used to treat acute respiratory failure in patients with cardiogenic pulmonary oedema, mainly in emergency departments. Investigators of several meta-analyses<sup>30–32</sup> concluded that this technique, including CPAP, is better than is standard medical therapy for reduction of intubation rate. Furthermore, they noted that CPAP reduces mortality. This conclusion was not supported in a multicentre trial<sup>33</sup> that compared oxygen therapy alone, CPAP, and non-invasive pressure support ventilation. The physiological improvements were faster with non-invasive ventilation than with oxygen alone but without a statistically significant effect on intubation or mortality rates. However, the very low intubation rate (<3%) raises questions as to whether the patients' population was similar to that of other studies.<sup>34–38</sup>

Meta-analyses<sup>30–32</sup> that compared non-invasive ventilation with CPAP alone in patients with cardiogenic pulmonary oedema showed that intubation and mortality rates did not differ, although investigators of some studies noted more rapid improvements in dyspnoea scores, oxygenation, and arterial partial pressure of carbon dioxide (PaCO<sub>2</sub>) with non-invasive ventilation than with CPAP. Nonetheless, because of ease of use, some clinicians regard CPAP as first-line treatment for cardiogenic pulmonary oedema in patients who do not

**Panel 2: Recommendations for NIV to treat acute respiratory failure**Recommendations based on levels of evidence<sup>21</sup>**Level 1 evidence**

Systematic reviews (with homogeneity) of RCTs and individual RCTs (with narrow CIs)

*Evidence of use (favourable)*

- COPD exacerbations
- Facilitation of weaning/extubation in patients with COPD
- Cardiogenic pulmonary oedema
- Immunosuppressed patients

*Evidence of use (caution)*

- None

**Level 2**

Systematic reviews (with homogeneity) of cohort studies—individual cohort studies (including low quality RCTs; eg, &lt;80% follow-up)

*Evidence of use (favourable)*

- Do-not-intubate status
- End-stage patients as palliative measure
- Extubation failure (COPD or congestive heart failure) (prevention)
- Community-acquired pneumonia in COPD
- Postoperative respiratory failure (prevention and treatment)
- Prevention of acute respiratory failure in asthma

*Evidence of use (caution)*

- Severe community acquired pneumonia
- Extubation failure (prevention)

**Level 3**

Systematic reviews (with homogeneity) of case-control studies, individual case-control study

*Evidence of use (favourable)*

- Neuromuscular disease/kyphoscoliosis
- Upper airway obstruction (partial)
- Thoracic trauma
- Treatment of acute respiratory failure in asthma

*Evidence of use (caution)*

- Severe acute respiratory syndrome

**Level 4**

Case series (and poor quality cohort and case-control studies)

*Evidence of use (favourable)*

- Very old age, older than age 75 years
- Cystic fibrosis
- Obesity hypoventilation

*Evidence of use (caution)*

- Idiopathic pulmonary fibrosis

NIV=non-invasive ventilation. RCTs=randomised controlled trials. COPD=chronic obstructive pulmonary disease.

have hypercapnoea.<sup>39</sup> According to the European Cardiology Task Force<sup>40</sup> for diagnosis and treatment of cardiogenic pulmonary oedema, non-invasive ventilation and CPAP are regarded as first-line treatments together with standard medical therapy when acute respiratory failure ensues.

Major abdominal and thoracic surgeries are often complicated postoperatively by hypoxaemia and respiratory failure, which is sometimes fatal. Pulmonary atelectasis after major surgery is frequent and might

predispose patients to pneumonia. In randomised trials CPAP reduced atelectasis and prevented pneumonia more effectively than did standard therapy after upper abdominal surgery,<sup>41</sup> and non-invasive ventilation substantially ameliorated gas exchange and abnormal changes in pulmonary function after gastrosplasty in patients who were obese.<sup>42</sup> Preventive use for a week before<sup>43</sup> or immediately after thoracic,<sup>44</sup> cardiac<sup>45</sup> or vascular<sup>46</sup> surgeries might mitigate loss of lung volume and development of atelectasis while easing recovery. Furthermore, use of non-invasive ventilation to treat early acute respiratory failure after lung resection improved survival in one randomised study.<sup>47</sup> These results lend support to use of CPAP or non-invasive ventilation in the postoperative setting, but more data are needed before specific recommendations can be made.

Acute respiratory failure in patients who are immunocompromised often signals a terminal phase of the underlying disease, with short survival time and high costs of admission to intensive care.<sup>48</sup> Early use of non-invasive ventilation could be very helpful, as shown by randomised studies in intensive care units that compared this technique with standard treatment. In patients receiving a solid-organ transplant and who had hypoxaemic acute respiratory failure, such ventilation reduced intubation rate, complications, mortality, and duration of stay in intensive care.<sup>49</sup> In a second study,<sup>50</sup> this technique lowered intubation, complication, and mortality rates compared with standard therapy in patients with hypoxaemia and bilateral pulmonary infiltrates and immunosuppression secondary to haematological malignancies, transplantation, or HIV infection. In view of the risk of admitting patients who are immunosuppressed to intensive care, some institutions now use non-invasive ventilation or CPAP early in haematology wards, either via a face mask or helmet, to avert transfer to intensive care.<sup>15</sup>

Obesity is an epidemic health and socioeconomic problem in many countries and predisposes people to chronic alveolar hypoventilation, usually in association with obstructive sleep apnoea. Obesity hypoventilation syndrome is defined as obesity with hypercapnia and can lead to acute respiratory acidosis during an exacerbation. Some case reports and observational studies suggest that non-invasive ventilation can ameliorate alveolar hypoventilation and avoid intubation in this situation.<sup>51,52</sup>

Patients with severe irreversible chronic diseases often eschew invasive mechanical ventilation when they present with acute respiratory failure and such ventilatory assistance might even be medically inappropriate for terminal stages.<sup>53</sup> Non-invasive ventilation could be used as an intermediate step to relieve symptoms and to achieve survival in hospital in some patients.<sup>54</sup> Two large US studies<sup>55,56</sup> in patients with acute respiratory failure and do-not-intubate orders reported that roughly half of those treated with this technique survived and were

discharged. Underlying disease was an important determinant of survival: patients with congestive heart failure had better survival rates than did those with COPD, and these rates were much better than were those for patients with pneumonia or cancer.

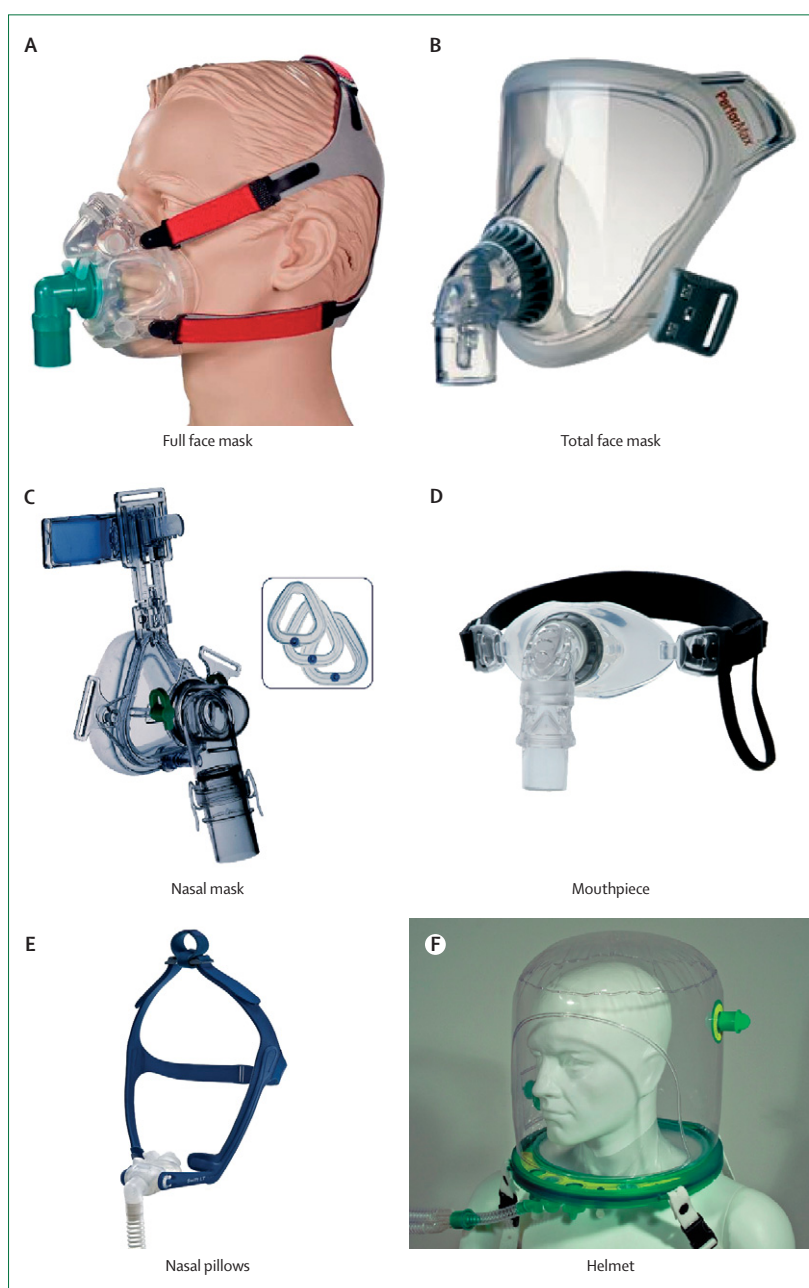
Observational studies found that non-invasive ventilation can be effective in relieving respiratory distress in patients admitted to either a respiratory unit<sup>57</sup> or a palliative care unit.<sup>16</sup> Early data from an ongoing multicentre randomised study<sup>58</sup> of non-invasive ventilation versus oxygen supplementation showed that it relieves signs of respiratory distress for at least 6 h after initiation and patients needed less morphine than did controls given oxygen. Patients with congestive heart failure and COPD who have do-not-intubate orders respond well to non-invasive ventilation, but use for other diagnoses and palliation, although appealing, needs further study.<sup>59</sup>

Two randomised controlled studies<sup>60,61</sup> assessed use of non-invasive ventilation during severe, non-life-threatening asthma attacks before development of acute respiratory failure. The first study<sup>60</sup> showed improved flow rates and reduced admissions with this technique compared with sham non-invasive ventilation. The second study<sup>61</sup> reported similar conclusions with high inflation pressures but not with low pressures or standard medical therapy. A trial can be considered for prevention of acute respiratory failure in patients with asthma who do not respond adequately to initial bronchodilator therapy. Whether this technique is effective for treatment of overt acute respiratory failure in patients with asthma is unknown.

A subset of patients—eg, those who are immunocompromised, have pneumonia and pulmonary fibrosis with a low ratio for arterial partial pressure of oxygen ( $\text{PaO}_2$ ) to fraction of inspired oxygen ( $\text{F}_i\text{O}_2$ ), or have bleeding diatheses—are at high risk for developing respiratory failure during fiberoptic bronchoscopy. Two randomised trials showed that either CPAP alone<sup>62</sup> or non-invasive ventilation<sup>62</sup> given via a full face mask improved oxygenation, and in one study<sup>63</sup> reduced postprocedure respiratory failure in patients with severe hypoxaemia. Similar findings with the helmet were reported.<sup>64</sup> Although evidence lends support to use of such ventilation during fiberoptic bronchoscopy to avoid intubation, close monitoring and ready availability of equipment for emergency intubation are necessary.

### Use within intensive care units

By contrast with use of non-invasive ventilation on a ward, the closely monitored intensive-care setting allows safe application of this technique even in very sick patients. To manage such patients non-invasively, including those with COPD exacerbations with severe respiratory acidosis (ie,  $\text{pH} < 7.30$ ), staff with much experience in this technique are needed, who are prepared to intubate promptly if goals are not met (ie, haemodynamic stability, adequate oxygenation, good cooperation).<sup>65,66</sup> Delays in intubation of these patients



**Figure: Different types of interfaces**

Images reproduced with permission from Hans-Rudolph (A), Respirationics (B), Koo Medical Equipment (C), Fisher & Paykel Healthcare (D), ResMed (E), and Harol (F).

runs the risk of unanticipated respiratory or cardiac arrest with attendant morbidity and mortality. Predictors of failure for non-invasive ventilation for hypercapnic respiratory failure are no improvement or a fall in  $\text{pH}$ , no change or a rise in breathing frequency after 1–2 h, high-acuity illness at admission (simplified acute physiology score II  $> 34$ ), and lack of cooperation. Predictors for hypoxaemic respiratory failure are no or a minimum rise in the ratio of  $\text{PaO}_2$  to  $\text{F}_i\text{O}_2$  after 1–2 h,



### Panel 3: Advantages and disadvantages of different types of interfaces

#### Total face mask—covers mouth, nose, and eyes

##### Advantages

- Minimum airleaks
- Little cooperation required
- Easy fitting and application

##### Disadvantages

- Vomiting (risk of aspiration)
- Claustrophobia
- Speaking difficult

#### Full face (or oronasal) mask—covers mouth and nose

##### Advantages

- Few air leaks
- Little cooperation required
- Can be adjusted for comfort

##### Disadvantages

- Vomiting
- Claustrophobia
- Possible nasal skin damage
- Speaking and coughing difficult

#### Nasal mask—covers nose and not mouth

##### Advantages

- Possibility of speaking and drinking
- Allows cough
- Reduced danger of vomiting
- Minimum risk of asphyxia

##### Disadvantages

- Air leaks if mouth opens
- Possible nasal skin damage
- Needs patent nasal passages

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(Continued from previous column)

#### Mouthpieces—placed between lips and held in place by lip seal

##### Advantages

- Can be applied as rotating strategy with other interfaces

##### Disadvantages

- Vomiting and salivation
- Possible air leaks
- Gastric distension
- Speaking difficult

#### Nasal pillows or plugs—inserted into nostrils

##### Advantages

- Can be applied as rotating strategy with other advantages of nasal masks
- Absence of nasal skin damage

##### Disadvantages

- Unreliable monitoring of expired tidal volume
- Inspiratory and expiratory air leaks
- Nasal irritation

#### Helmet—covers the whole head and all or part of the neck (no contact with face)

##### Advantages

- Minimum airleaks
- Little cooperation required
- Absence of nasal or facial skin damage

##### Disadvantages

- Rebreathing
- Vomiting
- Noisy
- Asynchrony with pressure support ventilation
- Discomfort of axillae (from straps)

patients older than 40 years (one study),<sup>67</sup> high acuity illness at admission (simplified acute physiology score >34), presence of acute respiratory distress syndrome, community acquired pneumonia with or without sepsis, and multiorgan system failure.

Hypoxaemic respiratory failure denotes patients with dyspnoea and tachypnoea with ratios of  $\text{PaO}_2$  to  $\text{F}_i\text{O}_2$  less than 200 and a non-COPD diagnosis such as pneumonia, acute respiratory distress syndrome, acute lung injury, or cardiogenic pulmonary oedema. Several clinical trials<sup>68–70</sup> have studied non-invasive ventilation in the intensive care unit to avoid intubation in such patients, but results are controversial. Major confounders of these studies were the large differences between enrolled patients in type of respiratory failure and severity of illness. For example, Confalonieri and colleagues<sup>71</sup> assessed use of this technique in patients with acute respiratory failure due to severe community-acquired pneumonia, including patients with and without COPD. Although non-invasive ventilation significantly reduced need for endotracheal intubation and length of hospital stay, in a subgroup analysis only patients with COPD

benefited. Observational studies<sup>72,73</sup> suggest that non-invasive ventilation is not useful for the avoidance of intubation when hypoxaemic acute respiratory failure is caused by community-acquired pneumonia in the absence of COPD.

Only one randomised trial<sup>74</sup> has thus far investigated use of this technique as an alternative to intubation in patients with hypoxaemic respiratory failure. Antonelli and co-workers<sup>74</sup> compared this technique with immediate intubation in patients with severe hypoxaemic respiratory failure who did not improve despite aggressive medical therapy. Oxygenation improved similarly within the first hour in both groups, and only 31% of patients in the non-invasive ventilation group needed intubation. Patients in the immediate intubation group developed serious complications, especially infections, more frequently than did those in the non-invasive group. In survivors, the duration of mechanical ventilation and stay in intensive care was shorter in those assigned to the non-invasive group.

Thus, although some studies suggest benefit, the use of non-invasive ventilation in acute respiratory distress

syndrome or severe community-acquired pneumonia is controversial and not recommended routinely.<sup>75</sup> Results of a survey<sup>76</sup> in three intensive care units, with staff highly skilled in this technique, showed that only 30% of patients with a diagnosis of acute respiratory distress syndrome met criteria for a trial of this type of ventilation. Of these patients, intubation was avoided in 54%, which was associated with much lowered morbidity (by about 40%) and mortality rates (roughly 30%). This finding suggests that in real-life situations and in expert hands only about 15% of such patients can be treated successfully with this technique; mainly those with a low severity of illness, not in shock, and rapid improvement in oxygenation after therapy is started.

Several randomised trials showed that non-invasive ventilation can be safely and successfully used to enable weaning from mechanical ventilation in stable patients recovering from an episode of hypercapnic acute respiratory failure (ie, COPD exacerbations)<sup>77,78</sup> and even in those who previously had an unsuccessful spontaneous breathing trial.<sup>79,80</sup> Respiratory failure after extubation occurs in about 15% of extubated patients, with an inhospital mortality that approaches 30–40%.<sup>81</sup> Two randomised trials<sup>82,83</sup> have shown that non-invasive ventilation applied immediately after extubation in patients considered at high risk of extubation failure (ie, elderly patients, and those with repeated failed weaning attempts, congestive heart failure, hypercapnia, hypoxaemia, acidaemia, and many comorbidities) lowered the rate of reintubation. Furthermore, in one study, mortality in the intensive care unit decreased in a subgroup of patients with hypercapnia.<sup>83</sup>

However, results from two previous randomised trials<sup>84,85</sup> showed no reduction in reintubation rates, and one<sup>85</sup> reported a significantly higher mortality in the intensive care unit in the non-invasive group, associated with longer delays in reintubation than in the control group (12 h vs 2 h). These findings led some researchers to conclude that non-invasive ventilation should not be used for extubation failure. However, only 10% of enrolled patients had COPD, perhaps predisposing to less favourable findings than seen in other studies. Furthermore, outcomes were improved in the group of controls who crossed over to non-invasive ventilation after they met criteria for respiratory failure, which suggests that some patients randomly assigned to this group started too early before they were clearly good candidates. Although controversial, accumulating evidence suggests that this technique has a role in treatment of extubation failure, but mainly in patients with hypercapnic and congestive heart failure who are at high risk for extubation failure. Furthermore, patients should be monitored closely to avoid delays in intubation.

Application of non-invasive ventilation for severe acute respiratory syndrome (SARS) and other airborne diseases has generated debate. On the basis of the

#### Panel 4: How to apply NIV during first few hours

- Explain technique to patient (if competent)
- Choose correct interfaces and size
- Set pressures starting from low levels (ie, pressure support about 8 cm H<sub>2</sub>O and external PEEP 4–5 cm H<sub>2</sub>O)
- Place interface gently over face, holding it in place and start ventilation
- When patient tolerant, tighten straps just enough to avoid major leaks, but not too tight
- Set F<sub>I</sub>O<sub>2</sub> on ventilator or add low-flow oxygen into the circuit, aiming for SO<sub>2</sub> > 90%
- Set alarms—low pressure alarm should be above PEEP level
- Be mindful of and try to optimise patient's comfort
- Reset pressures (pressure support increased to get expired tidal volume 6 mL/kg or higher—raise PEEP external to get oxygen saturation 90% or higher).
- Protect site of skin pressure from the interface (ie, artificial skin, wound-care dressing, or rotating interfaces)
- Consider use of mild sedation if patient is agitated
- Monitor comfort, respiratory rate, oxygen saturation, and dyspnoea every 30 min for 6–12 h then hourly
- Measure arterial blood gases at baseline and within 1 h from start
- Humidification advised for applications longer than 6 hours

NIV=non-invasive ventilation; PEEP=end-expiratory positive pressure; F<sub>I</sub>O<sub>2</sub>=fraction of inspired oxygen; SO<sub>2</sub>=oxygen saturation.

Toronto experience<sup>86</sup> with SARS, in which some caregivers contracted the syndrome when a patient was intubated after failure of non-invasive ventilation, use of this technique was discouraged for patients with this disease. However, two subsequent observational studies<sup>87,88</sup> from China reported no evidence of viral spread to caregivers who took appropriate precautions. In the event of an avian influenza pandemic, ventilator resources will probably be severely strained, and non-invasive ventilation might offer a means to support some affected patients. However, some clinicians consider this technique contraindicated in respiratory failure from communicable respiratory airborne diseases unless used inside a negative-pressure isolation room with strict precautions.

#### Methods, staffing, and costs

Although bulky and often cumbersome, negative-pressure ventilators such as the so-called iron lung are still used in some countries.<sup>89</sup> Non-invasive ventilation nowadays almost always consists of positive pressure delivered to the upper airway via a mask or other interface, and uses different physiological principles, dependent on the mode of delivery. During CPAP, a constant positive pressure is applied to raise functional residual capacity and open flooded alveoli in patients with cardiogenic pulmonary oedema. CPAP can lessen left ventricular transmural pressure, reducing afterload and increasing cardiac output, providing an additional rationale for use in the treatment of such patients.<sup>30,31</sup> CPAP can also be given via a helmet, which can cause difficulties with synchrony between the patient and ventilator when used with forms of positive-pressure ventilation that need triggering by the patient.<sup>30</sup>

	Reducing mortality	Decreasing intubation
COPD exacerbation <sup>11</sup>	+++	+++
CPO <sup>44</sup>	++	+++
Weaning COPD patients <sup>107*</sup>	+++	WMD -6.32
Miscellaneous hypoxic patients <sup>108</sup>	+	+

+=relative risk (RR) 71–84%. ++=RR 50–70%. +++=RR <50%. Data show effects on clinical outcomes according to meta-analysis of randomised controlled trials. COPD=chronic obstructive pulmonary disease. CPO=cardiogenic pulmonary oedema. WMD=weighted mean difference. \*Weighted mean difference on the duration of intubation (days) vs traditional weaning with the endotracheal tube.

**Table: Effects of non-invasive ventilation versus standard medical treatment**

Pressure-support ventilation assists inspiration via a preset positive-pressure boost triggered by the patient. The higher pressure is delivered until the inspiratory flow rate falls below a target pressure. In this way, pressure-support ventilation allows the patient to set not only breathing rate but also inspiratory and expiratory durations, the feature that distinguishes it from other ventilator modes. Bilevel ventilation, the combination of pressure support to reduce inspiratory work and extrinsic positive end-expiratory pressure to counterbalance intrinsic positive end-expiratory pressure, achieves a greater reduction in work of breathing than does either mode alone, at least in patients with COPD.<sup>91</sup>

Pressure-control ventilation,<sup>92</sup> like pressure-support ventilation, fluctuates between high inspiratory and low expiratory pressures, but contrasts with pressure-support ventilation in that the ventilator cycles into expiration when a preset inspiratory time is reached so that the patient is unable to control the duration of inspiration. Proportional-assist ventilation<sup>93</sup> targets spontaneous inspiratory flow rate as a surrogate of patients' effort and might improve synchrony between patient and ventilator and tolerance in some patients. Although this mode might be more comfortable and needs fewer adjustments than some pressure-support modes,<sup>93</sup> it is more complex to use than pressure-support ventilation and has not been widely adopted. Pressure-support ventilation, pressure-control ventilation, and proportional-assist ventilation have been used alone or in combination with extrinsic positive end-expiratory pressure in treatment of both acute hypoxic and hypercapnic respiratory failure.

Interfaces connect the patient's airway to the ventilator tubing. Six types of interfaces are commercially available that can be used to apply positive pressure to the upper airway during an episode of acute respiratory failure (figure): full-face (or oronasal) mask, total face mask, nasal mask, mouthpieces, nasal pillows or plugs, and a helmet. For acute applications, most clinicians use face masks (total or full), then nasal masks, and to a lesser extent other interfaces<sup>94</sup> (panel 3).

Nasal bridge ulcers develop less often than they did previously because of use of soft silicone seals, lessened

strap tension, and use of artificial skin at the first sign of skin reddening. Tightening straps excessively is strongly discouraged because of discomfort and risk of ulcers and air leaking might be increased.<sup>95</sup> Although full-face masks are tolerated better than nasal masks initially and are the preferred interface in the acute care setting,<sup>96</sup> both facial and nasal masks improve arterial blood gases equally<sup>97</sup> and patients might tolerate the nasal mask better than the face mask if they have claustrophobia or a frequent productive cough.<sup>98</sup>

Skill of the caregivers and their extent of experience in use of non-invasive ventilation are important to the success of this technique (panel 4).<sup>99,100</sup> Thus, as the skills of staff develop, they might be able to successfully treat very sick patients. Additionally, the use of protocols to guide use might improve selection of appropriate patients.<sup>101</sup> Although Chevrolet and co-workers<sup>102</sup> characterised non-invasive ventilation as excessively demanding on personnel time, subsequent studies<sup>26,103</sup> have shown that, despite taking about 30–60 min longer, initiation with invasive mechanical ventilation is rated by staff as no more difficult to administer than is invasive mechanical ventilation.

Optimum staffing and location for delivery depend on acuity of the patient and their severity of illness, monitoring capabilities of the unit, and experience of the staff.<sup>23</sup> Several factors should be considered before a patient is transferred from intensive care to a ward—eg, patients should not need invasive monitoring (arterial lines) or inotropes, nurse to patient ratio should be low (ie, more than one to four), and staffs' skill needs to be adequate to assess when non-invasive ventilation is failing and the patient needs to be transferred to a protected environment. Patients should be able to call for help if needed and pass a weaning test of more than 15 min without serious respiratory distress or oxygen desaturation. Finally, patients should have no need for high concentrations of oxygen supplementation (ie,  $F_{iO_2} > 60\%$ ).

Ventilators and monitoring systems have improved and might be important in the success of non-invasive ventilation. Specifically, most new ventilators have modes that compensate for air leaks, improved and sometimes adjustable triggering, systems to achieve best possible synchrony, and minimise rebreathing of carbon dioxide.<sup>104,105</sup> Additionally, humidification of the upper airway is important to improve comfort and tolerance. Heated passover humidifiers might reduce work of breathing and carbon dioxide accumulation compared with heat and moisture exchangers, mainly because dead space and resistance are lessened with the non-invasive technique.<sup>106</sup>

Effectiveness of non-invasive ventilation in specific diseases is well documented and quantified (table). Few studies have, however, systematically assessed the cost effectiveness of this technique. Keenan and colleagues<sup>109</sup> evaluated the health economics for severe acute

exacerbations of COPD with a theoretical model that used a decision-tree analysis constructed from a meta-analysis of randomised trials. They concluded that non-invasive ventilation was very cost-effective. Plant and co-workers<sup>110</sup> reported that when implemented on a ward, this technique reduces costs (by avoiding admission to intensive care) and improves outcomes compared with traditional medical treatment. Furthermore, the reduced rate of ventilator-associated pneumonia achieved with non-invasive ventilation not only offers clinical benefits for patients but also might have financial advantages for hospitals. For example, the cost of respiratory failure complicated by ventilator-associated pneumonia is very high, which creates a strong financial incentive for hospitals to prevent this potentially life-threatening and expensive complication.<sup>111</sup>

## Conclusion

Non-invasive ventilation has an important role in the management of respiratory failure in acute-care hospitals. Its use to treat acute respiratory failure related to COPD exacerbations, cardiogenic pulmonary oedema, and patients in immunosuppressed states has gained wide acceptance. Many other potential applications are undergoing further investigation. Furthermore, because intensive care units are often full, use of this technique in other settings is becoming common in many hospitals, but patients should be selected carefully to assure safety. We expect expanded use of non-invasive ventilation as new applications are explored and caregivers develop skill in the technique, but caution should be exercised to restrict use to appropriate applications (ie, avoiding patients with contraindications or excessive delays in intubation). Much variability exists between institutions in how often, with which mode, and in which setting this technique is applied and efforts should be made to ensure that acquisition of skills helps to narrow these differences.

## Contributors

SN undertook an independent database search, wrote and revised the manuscript, developed the figures, tables, and references list; and obtained copyright of images in figure 1. NSH did an independent database search, participated in writing, revision, and English checking of the manuscript, and revision of articles and figures.

## Conflicts of interest

SN has received honoraria from Respiromics and Resmed; travel grants from Fisher & Paykel, Respiromics, Resmed, Weinmann, Draeger; and free equipment from Fisher & Paykel, Respiromics, Resmed, Draeger, and Taema. NSH has received honoraria and research funding, and serves as a consultant and medical advisory board member for Respiromics.

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