# Non-invasive support for the hypoxaemic patient


## Abstract

Optimisation of oxygenation strategies in patients with hypoxaemic respiratory failure is a top priority for acute care physicians, as hypoxaemic respiratory failure is one of the leading causes of admission. Various oxygenation methods range from non-invasive face masks to high flow nasal cannulae, which have advantages and disadvantages for this heterogeneous patient group. Focus has turned toward examining the benefits of non-invasive ventilation, as this was heavily researched in resource-limited settings during the COVID-19 pandemic. The oxygenation strategy should be determined on an individualised basis for patients, and with new evidence from the COVID-19 pandemic, providers may now consider placing further emphasis on non-invasive approaches. As non-invasive ventilation continues to be used in increasing frequency, new methods of monitoring patient response, including when to escalate ventilation strategy, will need to be validated.



Key words: Acute hypoxaemic respiratory failure; High-flow nasal oxygen; Non-invasive ventilation

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## Epidemiology of acute hypoxic respiratory failure

Acute hypoxaemic respiratory failure is among the leading causes of intensive care unit admission in Canada and the USA, often resulting in the use of invasive mechanical ventilation (Barrett et al, 2014). Since the COVID-19 pandemic, there has been an increasing number of patients with acute hypoxaemic respiratory failure requiring intubation and mechanical ventilation (Docherty et al, 2021). Acute hypoxaemic respiratory failure is a poorly defined, heterogeneous syndrome caused by a variety of conditions, including pneumonia, cardiogenic pulmonary oedema, sepsis and septic shock, and trauma. The management of acute hypoxaemic respiratory failure is primarily supportive and focused on treating the underlying cause.

Traditional respiratory support with invasive mechanical ventilation, albeit lifesaving, is also associated with notable complications (Russotto et al, 2021). Therefore, less invasive methods to support oxygenation and ventilation have been developed. The COVID-19 pandemic, and the overwhelming strain it placed on intensive care units globally, further highlighted the need to identify strategies that reduce the demand for invasive mechanical ventilation, prompting the widespread adoption and evaluation of non-invasive respiratory strategies in acute hypoxaemic respiratory failure.

This article reviews the physiological underpinnings of non-invasive respiratory support, the pre-COVID-19 pandemic evidence that supported its adoption, and the evidence generated during COVID-19. Finally, future opportunities for research are proposed.

## Basic physiology of non-invasive support

Each non-invasive oxygenation device has unique physiological considerations and important advantages and disadvantages that must be understood to deliver safe, effective, and personalised therapy (Table 1). Matching the appropriate patient and clinical condition to a non-invasive oxygen strategy is imperative to derive optimal benefit.

### Non-invasive ventilation

In patients with acute respiratory failure, non-invasive ventilation is often delivered via a full oro-nasal facemask. Other non-invasive ventilation interfaces include a helmet apparatus, which has garnered much attention in recent years (Patel et al, 2016). Non-invasive ventilation


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**Table 1. Advantages and disadvantages of common non-invasive oxygen devices**

| Device | Advantages | Disadvantages |
|---|---|---|
| Non-invasive face mask | Alveolar recruitment optimised with pressure support<br>Oxygenation improved with positive end-expiratory pressure<br>Ability to monitor high tidal volumes<br>Decreases preload and afterload to improve cardiac function | Risk of aerosolisation<br>Positive end-expiratory pressure limited by air leaks<br>Many patients do not tolerate for long periods<br>Risk of skin ulceration<br>Risk of high tidal volumes or patient self-inflicted lung injury<br>Hospital transport challenges |
| Non-invasive helmet | Alveolar recruitment optimised with pressure support<br>Higher positive end-expiratory pressure than facemask non-invasive ventilation improves oxygenation<br>Higher patient tolerance allowing longer durations of therapy | Tidal volume cannot be assessed<br>Longer time needed to remove device in emergency situations<br>Staff have less familiarity with the device than facemask non-invasive ventilation at many institutions<br>Hospital transport challenges |
| High-flow nasal oxygen | Potential generation of small amounts of positive end-expiratory pressure<br>Mucociliary clearance enhanced by heated and humidified oxygen<br>Better tolerated, increased comfort<br>Decreased incorporation of room air<br>Dead-space washout<br>Work of breathing is decreased | Risk of aerosolisation<br>Hospital transport challenges<br>Very minimal generation of positive end-expiratory pressure<br>Discomfort when higher flows are used<br>Discomfort from heated humidification |

is delivered through bi-level positive airway pressure with inspiratory positive airway pressure and end-expiratory pressure, similar to positive end-expiratory pressure that is commonly used in invasive mechanical ventilation (Mehta and Hill, 2001). Physiologically, non-invasive ventilation increases airway pressure, improves arterial oxygenation, increases end-expiratory lung volume, and decreases the intrapulmonary shunt and expiratory diaphragm loading. Non-invasive ventilation may also improve cardiac performance by reducing left ventricular afterload and right and left ventricular preload (Mehta and Hill, 2001).

Additional considerations are needed in patients for whom sepsis is suspected, as a large study of patients with acute respiratory distress syndrome ($n$=4277) found sepsis was significantly associated with higher odds (odds ratio 4.47) of failure of non-invasive ventilation (Taha et al, 2019). Non-invasive ventilation may also be unsuitable for patients with excessive secretions, the inability to protect their airway, and facial trauma or surgery (Ambrosino and Vagheggini, 2008). Non-invasive ventilation delivered through a helmet has similar physiological benefits as that delivered via a facemask, but has the advantage of minimising substantial leak with a soft collar neck seal. This may result in more effective recruitment and enhanced titration of positive end-expiratory pressure. Furthermore, helmet non-invasive ventilation may be better tolerated, allowing longer duration of therapy.

## High-flow nasal oxygen

High-flow nasal oxygen is a method of oxygen delivery using an air-oxygen blender, heated humidifier, a heated inspiratory circuit and large-diameter nasal cannulae (Nishimura, 2016). With this, oxygen is safely delivered through the nose at high flow rates once it has been heated and humidified (Frat et al, 2015). Oxygen can be delivered with a more precise fraction of inspired oxygen ($FiO_2$) (Sztrymf et al, 2011) at a flow rate of up to 120 litres/min, compared to the maximum of 15 litres/min achieved with conventional oxygen therapy (Nishimura, 2016). With these high flow rates, there may be some degree of positive end-expiratory pressure, thoracoabdominal synchrony is improved, and carbon dioxide is

cleared from the upper airway and anatomical dead space (Nishimura, 2016). These factors may contribute to improved lung recruitment, higher partial pressure of oxygen/fraction of inspired oxygen ($PaO_2/FiO_2$), less dynamic strain and lower work of breathing (Frat et al, 2015; Nishimura, 2016; Mauri et al, 2017). The humidification of oxygen also contributes to better patient comfort when compared to delivery through a facemask (Frat et al, 2015).

## Evidence and indications for non-invasive oxygen strategies in acute hypoxaemic respiratory failure

### Undifferentiated acute hypoxaemic respiratory failure

As acute hypoxaemic respiratory failure remains a largely heterogeneous syndrome with varying pathophysiology, the ideal non-invasive oxygen strategy for undifferentiated acute hypoxaemic respiratory failure is controversial. Importantly, the response to a given non-invasive oxygenation strategy is likely driven by the severity and duration of illness as well as its underlying aetiology. For example, non-invasive ventilation was used in approximately 15% of patients in a large prospective cohort of patients with acute respiratory distress syndrome across 50 intensive care units globally. Failure of non-invasive ventilation occurred more frequently in patients with severe hypoxaemia (47%) than those with moderate (42%) or mild (22%) acute respiratory distress syndrome (Bellani et al, 2016).

To evaluate the role of non-invasive strategies in undifferentiated acute hypoxaemic respiratory failure, 313 patients with non-hypercapnic acute hypoxaemic respiratory failure across 23 intensive care units were recruited in a multicentre, randomised controlled trial, which compared standard facemask oxygen, facemask non-invasive ventilation and high-flow nasal oxygen (Frat et al, 2015). While the frequency of intubation was similar across groups (47%, 50% and 38% respectively; $P$=0.18), patients who received high-flow nasal oxygen had more ventilator-free days (24±8 days vs 22±10 days in the standard oxygen group and 19±12 days in the non-invasive ventilation group). Additionally, patients who received high-flow nasal oxygen had a significant reduction in 90-day mortality; the hazard ratio for death at 90 days was 2.01 (95% confidence interval 1.01–3.99) with standard oxygen compared to high-flow ($P$=0.046) and 2.50 (95% confidence interval 1.31–4.78) when non-invasive ventilation was compared with high-flow oxygen ($P$=0.006) (Frat et al, 2015). Use of high-flow nasal oxygen has increased rapidly as a result of this trial.

A subsequent network meta-analysis, which included 3804 patients with acute hypoxaemic respiratory failure across 25 studies, compared each non-invasive oxygen strategy (Ferreyro et al, 2020). Compared with standard oxygen, patients who received non-invasive ventilation via facemask not only had a lower risk of mortality (relative risk 0.83; 95% credible interval 0.68–0.99) but also a lower risk of intubation (relative risk 0.76; 95% credible interval 0.62–0.90). However, the mortality benefit was limited to patients with mild respiratory failure (mean $PaO_2/FiO_2$ >200). The interface of non-invasive ventilation may also be critical to its benefit. Non-invasive ventilation provided via the helmet interface was associated with lower risk of mortality and intubation relative to all other modalities studied, including standard oxygen, high-flow nasal oxygen, and facemask non-invasive ventilation. Importantly, no significant difference in the association with mortality or intubation was identified when facemask non-invasive ventilation was compared with high-flow nasal oxygen, albeit in a small number of studies.

### Hydrostatic pulmonary oedema

In patients with acute cardiogenic pulmonary oedema, both continuous positive airway pressure and bilevel non-invasive ventilation have been extensively studied. The largest trial spanned 26 emergency departments and randomised 1069 patients to standard oxygen, continuous positive airway pressure and bilevel non-invasive ventilation. No difference in mortality was identified at 30 days between groups (Gray et al, 2008). However, subsequent systematic reviews (Weng et al, 2010; Berbenetz et al, 2019) and a pooled analysis performed for a clinical practice guideline (Rochwerg et al, 2017) demonstrated meaningful reductions in mortality (relative risk 0.80, 95% confidence interval 0.66–0.96) and intubation (relative risk 0.60, 95% confidence interval 0.44–0.80), with similar effects seen using either bilevel non-invasive ventilation or continuous positive airway pressure.

## Immunocompromised patients

Non-invasive ventilation is widely used in immunocompromised, and particularly oncological patients. This is, in part, a result of historic reports of increased mortality associated with intubation and invasive mechanical ventilation in this population, and multiple early studies that demonstrated increased survival with non-invasive ventilation use in patients with both haematological and solid organ malignancies (Antonelli et al, 2000; Hilbert et al, 2001). Additionally, a propensity score analysis of 1302 patients with haematological malignancies in a large observational multicentre survey further demonstrated the association between the use of non-invasive ventilation and survival (Gristina et al, 2011).

Immunocompromised patients now face lower mortality when requiring ventilatory support, because of advances in the management of cancer care. In a large randomised controlled trial of early non-invasive ventilation vs conventional oxygen therapy, which included 374 immunocompromised patients admitted to the intensive care unit with acute hypoxaemic respiratory failure, there was no significant difference in 28-day mortality (non-invasive ventilation 24% vs conventional oxygen therapy 27%; $P$=0.47) or failure of the oxygen strategy (non-invasive ventilation 38% vs conventional oxygen therapy 48%; $P$=0.20) (Lemiale et al, 2015). Similarly, in a post-hoc analysis, non-invasive ventilation was not associated with improved survival among immunocompromised patients and was independently associated with an increased odds of intubation (Frat et al, 2016). Given the evolving evidence regarding non-invasive ventilation in oncological patients, high-flow nasal oxygen has emerged as a promising non-invasive oxygen strategy. While high-quality evidence is limited, Sklar et al (2018) summarised the existing literature, including both observational studies and randomised controlled trials, to assess the role of high-flow nasal oxygen compared to conventional oxygen therapy and non-invasive ventilation in immunocompromised patients. High-flow nasal oxygen was associated with both lower mortality (seven studies; 1429 patients, relative risk 0.72, 95% confidence interval 0.56–0.93, $P$=0.01) and lower rate of intubation (eight studies, 1529 patients, relative risk: 0.81, 95% confidence interval 0.67–0.96, $P$=0.02) than the oxygen control groups (conventional oxygen therapy and non-invasive ventilation). While high-flow nasal oxygen has significant potential for immunocompromised patients with acute hypoxaemic respiratory failure, a paucity of high-quality data persists, and further trials are required to guide its use.

## Chronic obstructive pulmonary disease

Numerous trials have demonstrated that bilevel non-invasive ventilation prevents intubation and confers survival benefit in patients with an exacerbation of chronic obstructive pulmonary disease (Brochard et al, 1995; Rochwerg et al, 2017). An improvement in acidosis and respiratory rate can often be seen within 4 hours of initiating therapy. However, in two large trials that compared non-invasive ventilation to first-line endotracheal intubation in patients with a lower average pH of 7.20, a significant mortality difference was not identified (Conti et al, 2002; Jurjević et al, 2009). Benefits in patients with severe acidosis included a reduction in length of hospital stay, complications and readmissions up to 1 year after discharge (Lindenauer et al, 2014). Therefore, clinical practice guidelines have strong recommendations for the use of bilevel non-invasive ventilation in patients with exacerbations of chronic obstructive pulmonary disease.

## Postoperative respiratory support

Atelectasis after surgery can result in acute hypoxaemic respiratory failure, and may be driven by pharmacodynamic properties of anaesthesia, postoperative pain and surgical location, namely intra-abdominal or intrathoracic surgery. In a multicentre randomised controlled trial of 298 patients with acute hypoxaemic respiratory failure after intra-abdominal surgery, non-invasive ventilation decreased the risk of both reintubation relative to conventional oxygen therapy (non-invasive ventilation 33%, conventional oxygen therapy 46%; $P$=0.03) and hospital-acquired infection (non-invasive ventilation 31%, conventional oxygen therapy 49%; $P$=0.03) (Jaber et al, 2016). These findings were consistent with multiple previous studies that assessed patients undergoing abdominal surgery (Jaber et al, 2005), solid organ transplantation (Antonelli et al, 2000) or those who received helmet non-invasive ventilation after abdominal surgery (Squadrone et al, 2005).

### Mitigation of reintubation after extubation

Despite fulfilling weaning criteria and a spontaneous breathing trial, as many as 23.5% of patients will fail extubation, resulting in hypoxaemic and/or hypercapnic respiratory failure (Boles et al, 2007). Importantly, patients who require reintubation often have worse outcomes, even after controlling for severity of illness (Thille et al, 2011). Therefore, patients at high risk of extubation failure, namely older adults or those with chronic cardiac or respiratory disease, may benefit from pre-emptive non-invasive oxygen support. Two multicentre randomised controlled trials assessed whether non-invasive ventilation could prevent reintubation when initiated soon after extubation. Nava et al (2005) randomised 97 patients to receive either conventional oxygen therapy or non-invasive ventilation for 8 hours per day for 2 days. They demonstrated a reduction in both reintubation and mortality. Similarly, Ferrer et al (2006) randomised 162 patients to conventional oxygen therapy or non-invasive ventilation for 24 hours continuously. While they demonstrated a reduction in mortality among those who received non-invasive ventilation, rates of reintubation were similar between groups.

Given its comfort and widespread availability, there has been a growing interest in the use of high-flow nasal oxygen to prevent extubation failure. In a large multicentre trial of 604 patients at high risk of extubation failure, high-flow nasal oxygen was found to be non-inferior to non-invasive ventilation for preventing reintubation (Hernández et al, 2016). A subsequent randomised controlled trial randomised 641 high-risk patients to receive high-flow nasal oxygen and non-invasive ventilation (for 12 hours per day) or high-flow nasal oxygen alone (for 48 hours post extubation), demonstrating that the combination of high-flow nasal oxygen and non-invasive ventilation significantly reduced the likelihood of reintubation (11.8% vs 18.2% in the high-flow nasal oxygen group) (Thille et al, 2019). Therefore, clinical practice guidelines recommend the use of non-invasive oxygen support in high-risk patients following extubation.

## Non-invasive oxygenation in COVID-19 patients

With surges of patients experiencing acute hypoxaemic respiratory failure during the COVID-19 pandemic, many hospitals were faced with the need to conserve ventilators. Conservation strategies provided a unique situation in which the benefits of non-invasive respiratory support via high-flow nasal oxygen or bilevel positive airway pressure/continuous positive airway pressure could be studied in patients with acute hypoxaemic respiratory failure or acute respiratory distress syndrome. Before the COVID-19 pandemic, a meta-analysis of randomised clinical trials showed lower risk of intubation in patients with hypoxaemic respiratory failure treated with high-flow nasal oxygen, helmet non-invasive ventilation or facemask non-invasive ventilation compared to those treated with standard oxygenation with nasal cannula (Ferreyro et al, 2020). Aside from resource conservation in the context of the COVID-19 pandemic, invasive ventilation also comes with risks such as barotrauma, which is particularly high in those with acute respiratory distress syndrome. One study found that COVID-19 patients with acute respiratory distress syndrome who underwent invasive ventilation were at a higher risk for barotrauma than those with acute respiratory distress syndrome from other causes (McGuinness et al, 2020). Patients with COVID-19 on high-flow nasal oxygen, continuous positive airway pressure or bilevel positive airway pressure were less likely to experience barotrauma in the form of subcutaneous emphysema, pneumothorax, or pneumomediastinum compared to those with invasive ventilation despite lung protective strategies (Rajdev et al, 2021).

While attempting to improve outcomes in non-intubated patients with oxygen requirements, some hospitals attempted self-proning. The largest randomised controlled trial of COVID-19 patients requiring high-flow nasal oxygen studied whether prone positioning decreased the rate of treatment failure, defined as intubation or mortality by 28 days (Ehrmann et al, 2021). Most instances of treatment failure were a result of the need for intubation, which occurred in 223 of 564 (40%) patients assigned to high-flow nasal oxygen with awake prone positioning and 257 (46%) of 557 patients assigned to high-flow nasal oxygen with standard care (relative risk 0.86; 95% confidence interval 0.75–0.98). The rates of adverse events, including vomiting, skin breakdown and central

or arterial line dislodgement, did not differ between the two groups (Ehrmann et al, 2021). Despite no obvious clinical benefit to awake self-proning, physiological variables, such as respiratory rate, ROX index (ratio of pulse oximetry/fraction of inspired oxygen ($SpO_2$/$FiO_2$) to respiratory rate) and oxygenation ($PaO_2$/$FiO_2$) all improved when transitioning from supine to prone position (Ehrmann et al, 2021). Criteria for determining optimal candidates for prone positioning vs proceeding to intubation have yet to be established.

When expanding the use of non-invasive oxygen strategies, many centres were forced to increase the use of high-flow nasal oxygen, including outside of the intensive care unit setting. Patients on high-flow nasal oxygen should be monitored closely because of the risk of desaturation from clinical worsening or disconnection. When intensive care unit beds were in high demand, patients on high-flow nasal oxygen were often put in specific high-flow nasal oxygen wards, general wards with continuous pulse oximetry and remote monitoring, or were risk stratified based on predicted need for intensive care. Before the COVID-19 pandemic, studies had begun on patients receiving high-flow nasal oxygen outside of the intensive care unit, with high-flow nasal oxygen-trained nurses. One study of 346 patients found that over half of these patients were able to avoid intensive care admission entirely (Jackson et al, 2021). The benefits of high-flow nasal oxygen use were seen during the COVID-19 pandemic as well; one randomised controlled trial studying high-flow nasal oxygen vs conventional oxygen therapy for patients with moderate COVID-19 pneumonia (blood oxygen saturation, $SpO_2$ of 90–94% on room air) showed that those on high-flow nasal oxygen had increased oxygenation ($PaO_2$/$FiO_2$), increased progression-free survival, and decreased time until de-escalation of oxygenation therapy (Nazir and Saxena, 2022).

The RECOVERY-RS randomised controlled trial included 1273 hospitalised adults with COVID-19-related acute hypoxaemic respiratory failure randomised to continuous positive airway pressure, high-flow nasal oxygen or conventional oxygen therapy (Perkins et al, 2022). The primary endpoints were requirement for invasive ventilation or mortality within 30 days, which was lower with continuous positive airway pressure (36.3%; 137 of 377 participants) vs conventional oxygen therapy (44.4%; 158 of 356 participants) (absolute difference −8%; 95% confidence interval −15% to −1%, $P$=0.03), but was not significantly different between high-flow nasal oxygen (44.3%; 184 of 415 participants) vs conventional oxygen therapy (45.1%; 166 of 368 participants) (absolute difference −1%; 95% confidence interval −8% to 6%, $P$=0.83) (Perkins et al, 2022). The difference in outcome between continuous positive airway pressure and conventional oxygen therapy was mainly driven by the decreased need for intubation. Importantly, adverse events such as pneumomediastinum, pneumothorax, and vomiting requiring emergent intubation were increased in the continuous positive airway pressure group. Of those who were eventually intubated, there was an increase in time until need for intubation in the continuous positive airway pressure vs conventional oxygen therapy group (median difference 1.0 day; 95% confidence interval 0.2–1.8 days) (Perkins et al, 2022).

Helmet non-invasive ventilation gained popularity during the COVID-19 pandemic. HENIVOT was the largest randomised controlled trial comparing helmet non-invasive ventilation to high-flow nasal oxygen in patients with COVID-19 (Grieco et al, 2021). Among 109 patients, they found no difference in the primary outcome of days free of respiratory support within 28 days of enrolment. However, there was a significant decrease in rate of intubation within 28 days in those in the helmet group vs high-flow nasal oxygen (30% vs 51%, absolute relative risk 21%, confidence interval 3–38%). When analysing clinical causes leading to intubation, those in the helmet group had significantly lower incidences of hypoxaemia, intolerable dyspnoea and respiratory muscle fatigue (Grieco et al, 2021).

Despite extensive research on the use of non-invasive respiratory support, no single strategy is clearly superior. A retrospective observational study of COVID-19 oxygenation strategies across 102 hospitals globally found that invasive ventilation rates and mortality rates were not correlated with the wide inter-hospital variation in rate of non-invasive ventilation or high-flow nasal oxygen use (Garcia et al, 2022). Clinical acumen is critical to determining the oxygenation strategy for each patient with individual needs and considerations.

## Future directions

As hospitals move towards increasing use of non-invasive respiratory support in patients with acute hypoxaemic respiratory failure, there are risks to consider, such as patient self-inflicted lung injury. In theory, patients with a high respiratory drive may inspire in a high-pressure, injurious manner, which is especially dangerous in the physiological setting of acute respiratory distress syndrome. Neuromuscular blockade decreases lung injury and the pro-inflammatory cytokine response (Forel et al, 2006) and thus improves survival in ventilated patients with acute respiratory distress syndrome (Papazian et al, 2010). To reduce the need for invasive ventilation, innovative approaches are needed to decrease patient self-inflicted lung injury without sedation and neuromuscular blockade. Tidal volume should be minimised in patients with acute respiratory distress syndrome, regardless of ventilation method, as increased tidal volume is significantly associated with failure of non-invasive ventilation (Carteaux et al, 2016). Although tidal volume may be assessed in bilevel ventilation, new monitoring strategies are being developed to assess tidal volume in non-invasive helmet ventilation (Cortegiani et al, 2019). Another way to decrease patient self-inflicted lung injury is through the application of positive end-expiratory pressure; this decreases atelectasis, spreads inspiratory stress more evenly and improves gas exchange to ultimately reduce the high respiratory effort (Battaglini et al, 2021).

As non-invasive ventilation and high-flow nasal oxygen are increasingly used outside of the intensive care setting, predictive scores can be helpful to stratify individual patients' risk of device failure. The ROX index has emerged as a tool to identify the likelihood of success of high-flow nasal oxygen. This may be of use in risk-stratifying patients for placement in high-flow nasal oxygen wards vs intensive care unit, as those with ROX > 4.88 at 2 hours, 6 hours or 12 hours after initiation have a significantly lower risk of intubation (Roca et al, 2019). During the COVID-19 pandemic, ROX >3 at 2 hours, 6 hours and 12 hours post-high-flow nasal oxygen initiation was shown to have a sensitivity of 85% for identifying high-flow nasal oxygen success (Chandel et al, 2021). Another method of predicting non-invasive ventilation failure is the HACOR score, which has been updated to improve predictive power. The HACOR score uses vital signs and arterial blood gas data, but the updated score also incorporates baseline condition variables (pulmonary acute respiratory distress syndrome, septic shock, immunosuppression, organ failure and presence of cardiopulmonary oedema) to improve predictive power (Duan et al, 2022). The updated HACOR score was validated across nine hospitals in 728 patients using non-invasive ventilation for hypoxaemic respiratory failure (Duan et al, 2022). Continual validation and updates to scores such as ROX and HACOR will help hospitals predict patient trajectory and improve stewardship of intensive care resources.

## Conclusions

There are several options for the treatment of acute hypoxaemic respiratory failure. Consideration of patient-specific factors during initial decision making and subsequent treatment evaluation is paramount for improving outcomes. The COVID-19 pandemic provided a unique opportunity for evaluation of non-invasive ventilation in patients hypoxaemic respiratory failure and overall illustrated its advantages in improving mortality rate and intubation risk in this population. Future priorities include standardising the selection method for oxygenation strategy, as well as the determinants of treatment failure requiring escalation to invasive mechanical ventilation.

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**Conflicts of interest**

The authors declare that there are no conflicts of interest.

## References


Ambrosino N, Vagheggini G. Noninvasive positive pressure ventilation in the acute care setting: where are we? Eur Respir J. 2008;31(4):874–886. https://doi.org/10.1183/09031936.00143507

Antonelli M, Conti G, Bufi M et al. Noninvasive ventilation for treatment of acute respiratory failure in patients undergoing solid organ transplantation: a randomized trial. JAMA. 2000;283(2):235–241. https://doi.org/10.1001/jama.283.2.235

Barrett ML, Smith MW, Elixhauser A, Honigman LS, Pines JM. Utilization of intensive care services, 2011, 2014. In: Healthcare cost and utilization project (HCUP) statistical briefs. Rockville (MD): Agency for Healthcare Research and Quality (US); 2014

Battaglini D, Robba C, Ball L et al. Noninvasive respiratory support and patient self-inflicted lung injury in COVID-19: a narrative review. Br J Anaesth. 2021;127(3):353–364. https://doi.org/10.1016/j.bja.2021.05.024

Bellani G, Laffey JG, Pham T et al. Epidemiology, patterns of care, and mortality for patients with acute respiratory distress syndrome in intensive care units in 50 countries. JAMA. 2016;315(8):788–800. https://doi.org/10.1001/jama.2016.0291

Berbenetz N, Wang Y, Brown J et al. Non-invasive positive pressure ventilation (CPAP or bilevel NPPV) for cardiogenic pulmonary oedema. Cochrane Database Syst Rev. 2019;(4):CD005351. https://doi.org/10.1002/14651858.CD005351.pub4

Boles J-M, Bion J, Connors A et al. Weaning from mechanical ventilation. Eur Respir J. 2007;29(5):1033–1056. https://doi.org/10.1183/09031936.00010206

Brochard L, Mancebo J, Wysocki M et al. Noninvasive ventilation for acute exacerbations of chronic obstructive pulmonary disease. N Engl J Med. 1995;333(13):817–822. https://doi.org/10.1056/NEJM199509283331301

Carteaux G, Millán-Guilarte T, De Prost N et al. Failure of noninvasive ventilation for de novo acute hypoxemic respiratory failure: role of tidal volume. Crit Care Med. 2016;44(2):282–290. https://doi.org/10.1097/CCM.0000000000001379

Chandel A, Patolia S, Brown AW et al. High-flow nasal cannula therapy in COVID-19: using the ROX index to predict success. Respir Care. 2021;66(6):909–919. https://doi.org/10.4187/respcare.08631

Conti G, Antonelli M, Navalesi P et al. Noninvasive vs. conventional mechanical ventilation in patients with chronic obstructive pulmonary disease after failure of medical treatment in the ward: a randomized trial. Intensive Care Med. 2002;28(12):1701–1707. https://doi.org/10.1007/s00134-002-1478-0

Cortegiani A, Navalesi P, Accurso G et al. Tidal volume estimation during helmet noninvasive ventilation: an experimental feasibility study. Sci Rep. 2019;9(1):17324. https://doi.org/10.1038/s41598-019-54020-5

Docherty AB, Mulholland RH, Lone NI et al. Changes in in-hospital mortality in the first wave of COVID-19: a multicentre prospective observational cohort study using the WHO Clinical Characterisation Protocol UK. Lancet Respir Med. 2021;9(7):773–785. https://doi.org/10.1016/S2213-2600(21)00175-2

Duan J, Chen L, Liu X et al. An updated HACOR score for predicting the failure of noninvasive ventilation: a multicenter prospective observational study. Crit Care. 2022;26(1):196. https://doi.org/10.1186/s13054-022-04060-7

Ehrmann S, Li J, Ibarra-Estrada M et al. Awake prone positioning for COVID-19 acute hypoxaemic respiratory failure: a randomised, controlled, multinational, open-label meta-trial. Lancet Respir Med. 2021;9(12):1387–1395. https://doi.org/10.1016/S2213-2600(21)00356-8

Ferrer M, Valencia M, Nicolas JM et al. Early noninvasive ventilation averts extubation failure in patients at risk: a randomized trial. Am J Respir Crit Care Med. 2006;173(2):164–170. https://doi.org/10.1164/rccm.200505-718OC

Ferreyro BL, Angriman F, Munshi L et al. Association of noninvasive oxygenation strategies with all-cause mortality in adults with acute hypoxemic respiratory failure: a systematic review and meta-analysis. JAMA. 2020;324(1):57–67. https://doi.org/10.1001/jama.2020.9524

Forel J-M, Roch A, Marin V et al. Neuromuscular blocking agents decrease inflammatory response in patients presenting with acute respiratory distress syndrome. Crit Care Med. 2006;34(11):2749–2757. https://doi.org/10.1097/01.CCM.0000239435.87433.0D

Frat J-P, Thille AW, Mercat A et al. High-flow oxygen through nasal cannula in acute hypoxemic respiratory failure. N Engl J Med. 2015;372(23):2185–2196. https://doi.org/10.1056/NEJMoa1503326

Frat J-P, Ragot S, Girault C et al. Effect of non-invasive oxygenation strategies in immunocompromised patients with severe acute respiratory failure: a post-hoc analysis of a randomised trial. Lancet Respir Med. 2016;4(8):646–652. https://doi.org/10.1016/S2213-2600(16)30093-5

Garcia MA, Johnson SW, Sisson EK et al. Variation in use of high-flow nasal cannula and noninvasive ventilation among patients with COVID-19. Respir Care. 2022;67(8):929–938. https://doi.org/10.4187/respcare.09672

Gray A, Goodacre S, Newby DE et al. Noninvasive ventilation in acute cardiogenic pulmonary edema. N Engl J Med. 2008;359(2):142–151. https://doi.org/10.1056/NEJMoa0707992

Grieco DL, Menga LS, Cesarano M et al. Effect of helmet noninvasive ventilation vs high-flow nasal oxygen on days free of respiratory support in patients with COVID-19 and moderate to severe hypoxemic respiratory failure: the HENIVOT randomized clinical trial. JAMA. 2021;325(17):1731–1743. https://doi.org/10.1001/jama.2021.4682

Gristina GR, Antonelli M, Conti G et al. Noninvasive versus invasive ventilation for acute respiratory failure in patients with hematologic malignancies: a 5-year multicenter observational survey. Crit Care Med. 2011;39(10):2232–2239. https://doi.org/10.1097/CCM.0b013e3182227a27

Hernández G, Vaquero C, Colinas L et al. Effect of postextubation high-flow nasal cannula vs noninvasive ventilation on reintubation and postextubation respiratory failure in high-risk patients: a randomized clinical trial. JAMA. 2016;316(15):1565–1574. https://doi.org/10.1001/jama.2016.14194

Hilbert G, Gruson D, Vargas F et al. Noninvasive ventilation in immunosuppressed patients with pulmonary infiltrates, fever, and acute respiratory failure. N Engl J Med. 2001;344(7):481–487. https://doi.org/10.1056/NEJM200102153440703

Jaber S, Delay J-M, Chanques G et al. Outcomes of patients with acute respiratory failure after abdominal surgery treated with noninvasive positive pressure ventilation. Chest. 2005;128(4):2688–2695. https://doi.org/10.1378/chest.128.4.2688

Jaber S, Lescot T, Futier E et al. Effect of noninvasive ventilation on tracheal reintubation among patients with hypoxemic respiratory failure following abdominal surgery: a randomized clinical trial. JAMA. 2016;315(13):1345–1353. https://doi.org/10.1001/jama.2016.2706

Jackson JA, Spilman SK, Kingery LK et al. Implementation of high-flow nasal cannula therapy outside the intensive care setting. Respir Care. 2021;66(3):357–365. https://doi.org/10.4187/respcare.07960

Jurjević M, Matić I, Sakić-Zdravcević K et al. Mechanical ventilation in chronic obstructive pulmonary disease patients, noninvasive vs. invasive method (randomized prospective study). Coll Antropol. 2009;33(3):791–797

Lemiale V, Mokart D, Resche-Rigon M et al. Effect of noninvasive ventilation vs oxygen therapy on mortality among immunocompromised patients with acute respiratory failure: a randomized clinical trial. JAMA. 2015;314(16):1711–1719. https://doi.org/10.1001/jama.2015.12402

Lindenauer PK, Stefan MS, Shieh M-S et al. Outcomes associated with invasive and noninvasive ventilation among patients hospitalized with exacerbations of chronic obstructive pulmonary disease. JAMA Intern Med. 2014;174(12):1982–1993. https://doi.org/10.1001/jamainternmed.2014.5430

Mauri T, Alban L, Turrini C et al. Optimum support by high-flow nasal cannula in acute hypoxemic respiratory failure: effects of increasing flow rates. Intensive Care Med. 2017;43(10):1453–1463. https://doi.org/10.1007/s00134-017-4890-1

McGuinness G, Zhan C, Rosenberg N et al. Increased incidence of barotrauma in patients with COVID-19 on invasive mechanical ventilation. Radiology. 2020;297(2):E252–E262. https://doi.org/10.1148/radiol.2020202352

Mehta S, Hill NS. Noninvasive ventilation. Am J Respir Crit Care Med. 2001;163(2):540–577. https://doi.org/10.1164/ajrccm.163.2.9906116

Nava S, Gregoretti C, Fanfulla F et al. Noninvasive ventilation to prevent respiratory failure after extubation in high-risk patients. Crit Care Med. 2005;33(11):2465–2470. https://doi.org/10.1097/01.ccm.0000186416.44752.72

Nazir N, Saxena A. The effectiveness of high-flow nasal cannula and standard non-rebreathing mask for oxygen therapy in moderate category COVID-19 pneumonia: randomised controlled trial. Afr J Thorac Crit Care Med. 2022;28(1):9–14. https://doi.org/10.7196/AJTCCM.2022.v28i1.206

Nishimura M. High-flow nasal cannula oxygen therapy in adults: physiological benefits, indication, clinical benefits, and adverse effects. Respir Care. 2016;61(4):529–541. https://doi.org/10.4187/respcare.04577

Papazian L, Forel J-M, Gacouin A et al. Neuromuscular blockers in early acute respiratory distress syndrome. N Engl J Med. 2010;363(12):1107–1116. https://doi.org/10.1056/NEJMoa1005372

Patel BK, Wolfe KS, Pohlman AS, Hall JB, Kress JP. Effect of noninvasive ventilation delivered by helmet vs facemask on the rate of endotracheal intubation in patients with acute respiratory distress syndrome: a randomized clinical trial. JAMA. 2016;315(22):2435–2441. https://doi.org/10.1001/jama.2016.6338

Perkins GD, Ji C, Connolly BA et al. Effect of noninvasive respiratory strategies on intubation or mortality among patients with acute hypoxemic respiratory failure and COVID-19: the RECOVERY-RS randomized clinical trial. JAMA. 2022;327(6):546–558. https://doi.org/10.1001/jama.2022.0028

Rajdev K, Spanel AJ, McMillan S et al. Pulmonary barotrauma in COVID-19 patients with ARDS on invasive and non-invasive positive pressure ventilation. J Intensive Care Med. 2021;36(9):1013–1017. https://doi.org/10.1177/08850666211019719

Roca O, Caralt B, Messika J et al. An index combining respiratory rate and oxygenation to predict outcome of nasal high-flow therapy. Am J Respir Crit Care Med. 2019;199(11):1368–1376. https://doi.org/10.1164/rccm.201803-0589OC

Rochwerg B, Brochard L, Elliott MW et al. Official ERS/ATS clinical practice guidelines: noninvasive ventilation for acute respiratory failure. Eur Respir J. 2017;50(2):1602426. https://doi.org/10.1183/13993003.02426-2016

Russotto V, Myatra SN, Laffey JG et al. Intubation practices and adverse peri-intubation events in critically III patients from 29 countries. JAMA. 2021;325(12):1164–1172. https://doi.org/10.1001/jama.2021.1727

Sklar MC, Mohammed A, Orchanian-Cheff A et al. The impact of high-flow nasal oxygen in the immunocompromised critically III: a systematic review and meta-analysis. Respir Care. 2018;63(12):1555–1566. https://doi.org/10.4187/respcare.05962

Squadrone V, Coha M, Cerutti E et al. Continuous positive airway pressure for treatment of postoperative hypoxemia: a randomized controlled trial. JAMA. 2005;293(5):589–595. https://doi.org/10.1001/jama.293.5.589

Sztrymf B, Messika J, Bertrand F et al. Beneficial effects of humidified high flow nasal oxygen in critical care patients: a prospective pilot study. Intensive Care Med. 2011;37(11):1780–1786. https://doi.org/10.1007/s00134-011-2354-6

Taha A, Larumbe-Zabala E, Abugroun A et al. Outcomes of noninvasive positive pressure ventilation in acute respiratory distress syndrome and their predictors: a national cohort. Crit Care Res Pract. 2019;2019:1–8. https://doi.org/10.1155/2019/8106145

Thille AW, Harrois A, Schortgen F, Brun-Buisson C, Brochard L. Outcomes of extubation failure in medical intensive care unit patients. Crit Care Med. 2011;39(12):2612–2618. https://doi.org/10.1097/CCM.0b013e3182282a5a

Thille AW, Muller G, Gacouin A et al. Effect of postextubation high-flow nasal oxygen with noninvasive ventilation vs high-flow nasal oxygen alone on reintubation among patients at high risk of extubation failure: a randomized clinical trial. JAMA. 2019;322(15):1465–1475. https://doi.org/10.1001/jama.2019.14901

Weng C-L, Zhao Y-T, Liu Q-H et al. Meta-analysis: noninvasive ventilation in acute cardiogenic pulmonary edema. Ann Intern Med. 2010;152(9):590–600. https://doi.org/10.7326/0003-4819-152-9-201005040-00009