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2 **British Thoracic Society Clinical statement on the use and monitoring of High**
3 **Flow Nasal Therapy (HFNT) in adult patients**
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Abbreviations List

ADRT:	advance decision to refuse treatment
AECOPD:	acute exacerbation of chronic obstructive pulmonary disease
AE-IPF:	acute exacerbation of idiopathic pulmonary fibrosis
AHRF:	acute hypercapnic respiratory failure
APACHE II:	Acute Physiology and Chronic Health Evaluation II
ARF:	acute respiratory failure
BMI:	body mass index
BTS:	British Thoracic Society
CAP:	community-acquired pneumonia
CHRF:	chronic hypercapnic respiratory failure
CI:	confidence interval
COPD:	chronic obstructive pulmonary disease
COT:	conventional oxygen therapy
CPAP:	continuous positive airway pressure
CrI:	credible interval
DNI:	do not intubate
DVT:	deep vein thrombosis
ED:	emergency department
FiO ₂ :	fraction of inspired oxygen
ERS:	European Respiratory Society
HFNT:	high-flow nasal therapy
HDU:	high dependency unit
HCP:	healthcare professional
HR:	hazard ratio
HRQoL:	health-related quality of life
ICER:	incremental cost-effectiveness ratio
ICS:	Intensive Care Society
ICU:	intensive care unit
ILD:	interstitial lung disease
IMV:	invasive mechanical ventilation
IPF:	idiopathic pulmonary fibrosis
LOS:	length of stay
LPA:	lasting power of attorney
LTOT:	long-term oxygen therapy

- 86 MCA: Mental Capacity Act
87 MDT: multidisciplinary team
88 NEWS2: National Early Warning Score 2
89 NIV: non-invasive ventilation
90 OSA: obstructive sleep apnoea
91 OR: odds ratio
92 PaCO₂: arterial partial pressure of carbon dioxide
93 PaO₂: arterial partial pressure of oxygen
94 PE: pulmonary embolism
95 QALY: quality-adjusted life year
96 RCT: randomised controlled trial
97 ROX index: respiratory rate–oxygenation index
98 RR: respiratory rate
99 RSU: respiratory support unit
100 RV: right ventricular
101 SGRQ: St George's Respiratory Questionnaire
102 SpO₂: peripheral oxygen saturation
103 VAP: ventilator-associated pneumonia
104 VTE: venous thromboembolism

Section 1: Summary of clinical practice points

Acute hypoxaemic respiratory failure: HFNT compared with COT, NIV and CPAP

- HFNT may be considered over COT where adequate oxygenation cannot be maintained, but CPAP/NIV may be more appropriate where positive pressure, alveolar recruitment, or ventilatory support is required.
- HFNT may be considered as an alternative to NIV in selected patients with hypoxaemic ARF where positive-pressure or ventilatory support is not specifically required, taking account of clinical trajectory and patient tolerance.
- Patient comfort should be considered when selecting respiratory support; however, this should not supersede clinical indications for NIV, CPAP or IMV where these are required.
- HFNT may be better tolerated than NIV.
- There is little evidence to support the use of HFNT compared to other methods of oxygen delivery in patients who are not suitable for intubation and ventilation.

Specific clinical conditions: mortality and risk of endotracheal intubation

Immunocompromised

- HFNT may be considered in immunocompromised patients with hypoxaemic ARF. Current evidence does not demonstrate a mortality benefit, while evidence for reducing intubation compared with COT is inconsistent.

COVID-19

- HFNT can safely be used in patients with hypoxaemic ARF secondary to COVID-19. It may be more effective than COT in reducing risk for intubation, but CPAP/NIV are at least as effective and may support oxygen delivery better in some patients.
- Patient choice and tolerance need consideration when making management decisions to treat hypoxaemic ARF in COVID-19 patients.

Interstitial lung disease

- HFNT may be considered on an individualised basis in ILD-related hypoxaemic ARF where a potentially reversible contributor is being treated, recognising the limited evidence of clinical benefit and poor prognosis, particularly in advanced fibrotic disease.
- HFNT may support palliative care in patients with ILD-related hypoxaemic ARF by improving symptom control, facilitating communication, and allowing time for patient/family discussions.
- Institution of HFNT in patients with ILD should include a weaning plan for respiratory support, developed with palliative care input.

Cardiogenic pulmonary oedema

- HFNT should be considered over COT to treat ARF in patients with acute cardiogenic pulmonary oedema to reduce work of breathing, improve oxygenation and reduce risk of intubation.

- No clear superiority of HFNT over CPAP/NIV has been established.
- HFNT in patients with cardiogenic pulmonary oedema should be delivered in a critical care setting or a high monitoring area such as a coronary care unit.

Asthma

- HFNT has not demonstrated an improvement in oxygenation, risk of IMV or hospital LOS compared with COT, but limited evidence from small trials suggests possible improvement in dyspnoea.
- If non-invasive respiratory support is applied in acute asthma, this should only be undertaken in a critical care environment to monitor for treatment failure and to enable rapid endotracheal intubation.

Pulmonary embolism

- HFNT could be considered to treat hypoxaemic ARF in patients with acute PE to reduce respiratory rate and work of breathing and improve oxygenation.
- HFNT in patients with acute PE should be delivered in a critical care setting or a high monitoring area.

Bronchiectasis

- HFNT may be considered as an adjunct in selected patients with bronchiectasis exacerbations and ARF where oxygenation, comfort or secretion clearance are problematic; however, evidence is indirect and limited.

Acute hypercapnic respiratory failure

Compared with COT

- NIV remains first-line for treatment of acidaemic AHRF.
- HFNT should not be routinely used in patients with compensated AHRF to prevent progression of hypercapnia.
- HFNT may be considered in selected patients with mild COPD-related AHRF, particularly where controlled oxygen delivery is required and there is no acidaemia.
- HFNT should not delay escalation to NIV where NIV is clinically indicated, particularly in patients with pH <7.35, worsening acidaemia, rising PaCO₂, increasing work of breathing or clinical deterioration.
- HFNT is not recommended as primary ventilatory support for AHRF due to neuromuscular disease, chest wall disease, severe obesity-related respiratory failure, or other causes of ventilatory failure where NIV is indicated.
- Patients should be managed with target oxygen saturations of 88–92% in known or suspected hypercapnia.
- Early reassessment (within 1–2 hours) is essential to identify non-responders.
- HFNT use in hypercapnia should only occur with a clear escalation plan specifying when NIV or IMV should be instituted, where appropriate.

- Patients receiving HFNT should be closely monitored for rising PaCO₂, respiratory fatigue, or progression of acidaemia.

Compared with NIV

- NIV should remain first-line therapy for AHRF with acidaemia (pH <7.35).
- HFNT should not be used as a replacement for NIV in acidaemic AHRF.
- HFNT may be considered where NIV is not tolerated or is contraindicated, but supporting clinical evidence is limited and low certainty.
- In patients with acidaemic AHRF who remain eligible for IMV, HFNT should only be considered where NIV is not tolerated or cannot be delivered. This should be delivered in a critical care setting with close monitoring and immediate access to intubation, as HFNT must not delay IMV where clinically indicated.

During planned NIV breaks

- Based on limited evidence, HFNT may be considered on an individualised basis during planned NIV breaks to improve comfort and tolerance, while maintaining oxygenation and supporting CO₂ washout.
- HFNT should not replace NIV unless there is clear intolerance or contraindication.
- NIV should be restarted promptly if hypercapnia worsens during HFNT use on blood gas or transcutaneous CO₂ monitoring, or if work of breathing increases.

Comfort, tolerance and patient experience

- HFNT settings should be individualised and titrated to patient comfort and work of breathing.
- Flow rates ≥30 L/min should generally be used to achieve physiological effect.
- Temperature and humidity settings may require adjustment during treatment and recovery according to patient tolerance and secretion burden.
- Comfort should not supersede clinical indications for NIV when required.

Practical aspects of acute respiratory failure

- HFNT is a high-risk therapy indicative of severe acute respiratory failure.
- Early senior clinical review should occur in all patients initiated on HFNT.
- HFNT should be delivered in enhanced monitoring environments such as RSU, HDU, ICU, coronary care or equivalent areas with trained staff and escalation pathways.
- Delivery in standard unenhanced ward environments without adequate monitoring, trained staff and escalation pathways is not appropriate for patients with significant oxygen requirements or clinical instability.
- The BTS/ICS RSU guidance specifically states that the minimum ratio recommended for an RSU is 1:4, with more staff required as acuity increases.
- HFNT must only be initiated with a documented escalation plan agreed by a senior clinician (ST3+/respiratory or critical care equivalent).

- Escalation plans should define:
 - suitability for NIV
 - suitability for IMV
 - any agreed limits to treatment escalation, where appropriate
 - palliative care strategy and weaning or withdrawal plan where NIV or IMV is not appropriate
- Failure to respond should prompt early senior review, with timely escalation of respiratory support or transition to symptom-focused palliative care in accordance with the agreed treatment escalation plan.
- Local HFNT protocols should include objective reassessment criteria, such as serial ROX index measurement in hypoxaemic ARF, alongside clinical assessment of work of breathing, oxygen requirement, gas exchange and mental status.
- All institutions using HFNT should maintain a formal HFNT policy, including:
 - indications and contraindications
 - initiation pathway or flowchart
 - initiation protocols
 - monitoring requirements
 - definition of HFNT failure
 - escalation and ceiling-of-care pathways
 - weaning strategies
- HFNT use should be evaluated in routine audit and morbidity/mortality review processes.
- Staff delivering HFNT must demonstrate documented competency-based training.
- HFNT should be integrated into structured acute respiratory failure pathways, not used as an isolated therapy.
- Oxygen infrastructure must support safe delivery of multiple high-flow devices where used at scale.
- HFNT should not delay escalation to ventilatory support such as NIV or IMV when clinically indicated.

Domiciliary HFNT in chronic respiratory failure

Chronic hypoxaemic respiratory failure

- Home HFNT may be considered as an adjunct to LTOT in selected patients with stable COPD and chronic hypoxaemic respiratory failure to reduce exacerbation frequency and improve symptom control.
- Home HFNT could be considered in selected patients with bronchiectasis and ILD, but evidence is currently insufficient to recommend its routine use; where considered, treatment should form part of a specialist-led, individualised clinical management plan.
- The practical utility of HFNT is limited by the requirement for a power supply and circuit length.
- Early involvement of palliative teams should be considered when starting home HFNT in patients with advanced, progressive or life-limiting respiratory disease.

- An action plan for device management including servicing, failure, cleaning, and backup during disruption to power supply should be instituted prior to initiating home HFNT.

Chronic hypercapnic respiratory failure

- NIV remains the standard of care for patients with CHRF.
- Home HFNT may be considered in selected patients with stable COPD and CHRF where NIV is not tolerated or accepted; however, evidence specifically evaluating HFNT following NIV intolerance or failure is very limited, and NIV remains the established standard of care.
- Monitoring should be tailored to identify treatment failure, with individualised failure criteria and escalation plans based on the patient's clinical context and suitability for further respiratory support.
- There is insufficient evidence to advocate for home HFNT in stable COPD patients with PaCO₂ >7.0 kPa, persistent hypercapnia following an exacerbation with AHRF, COPD–OSA overlap, obesity-related respiratory failure, neuromuscular disease or other non-COPD causes of chronic hypercapnic respiratory failure.

Practical aspects of managing HFNT in community settings

- Home HFNT delivery should involve liaison between acute and community multidisciplinary teams to support safe setup, clinical oversight and continuity of care.
- Transport of patients dependent on HFNT should be undertaken by appropriately trained transport or ambulance teams, with detailed handover to the receiving community team.
- Care plans should be developed for device management, transport and contingencies during device or power failure.
- Commissioning arrangements should be proportional to the complexity of the management of the home HFNT service and dependent on the local funding model.

Secretion management

- There is a paucity of high-quality clinical trials evaluating HFNT for secretion management in both acute and chronic respiratory disease.
- HFNT should not be initiated primarily or solely for mucus clearance in acute respiratory failure.
- HFNT should not be initiated primarily or solely for mucus clearance in the domiciliary setting outside specialist respiratory supervision.
- Established physiotherapy-led ACTs should remain the primary airway-clearance strategy, while HFNT should be considered an adjunct rather than a replacement.

301 Withdrawal and palliation

- 302 • HFNT withdrawal should occur within a structured multidisciplinary and palliative care
303 framework, with senior clinical leadership and early specialist palliative care
304 involvement.
- 305 • Withdrawal planning should consider the distinction between oxygenation-dependent
306 and symptom-control–dependent patients.
- 307 • Capacity assessment and legal frameworks (ADRT, LPA, MCA 2005) must be followed
308 and documented.
- 309 • Withdrawal planning should include anticipatory prescribing for dyspnoea, anxiety, and
310 terminal agitation.
- 311 • Non-pharmacological measures for symptom management, including fan therapy,
312 mouth care and environmental optimisation, should be routinely used.
- 313 • Monitoring should prioritise comfort and symptom burden rather than physiological
314 targets.
- 315 • Escalation pathways must be clearly defined, including access to senior clinicians and
316 palliative care teams.
- 317 • Withdrawal may occur in hospital, hospice, or home settings depending on patient
318 preference and clinical stability.
- 319 • Some patients may continue HFNT until death where symptom benefit outweighs
320 burdens.
- 321 • Clear documentation of decision-making, rationale, and care plans is essential.
- 322 • Complex or disputed decisions should prompt senior multidisciplinary review and,
323 where appropriate, independent clinical or ethics support; unresolved significant
324 disagreement may require legal advice or referral to the Court of Protection.

Section 2: Introduction, scope and methodology

Introduction

High Flow Nasal Therapy (HFNT) is a non-invasive respiratory therapy administered through a nasal cannula that delivers heated and humidified room air. Oxygen can be entrained to deliver a stable fraction of inspired oxygen (FiO₂) up to 100% at flow rates of up to 60 L/min in routine clinical practice.¹ HFNT may also be delivered through a tracheostomy interface in selected patients.² HFNT is applied in clinical practice to support patients in the acute inpatient and stable home settings, to provide respiratory support for the management of respiratory failure, airway clearance and breathlessness in a range of underlying conditions.^{3,4} This British Thoracic Society (BTS) Clinical Statement aims to address the role of HFNT in a variety of scenarios with additional recommendations/descriptions on monitoring, safety and practical delivery, with key clinical practice points in each of the sections. The lack of robust evidence for several clinical applications is acknowledged. In areas where evidence is significantly lacking, expert opinion is provided along with research direction to address the evidence gap.

This statement was commissioned to address increasing clinical applications of HFNT, including areas where robust evidence is lacking. The purpose of this clinical statement is to provide an overview of clinical scenarios where HFNT could be applied, evidence supporting such application or expert opinion where robust clinical trial evidence is lacking, research recommendations, and clinical practice points for the general respiratory clinician. A summary of clinical practice points is provided in Section 1. Evidence summary tables are provided in Appendix 1.

Scope

This clinical statement covers a broad range of clinical conditions where HFNT use is prevalent. This includes acute and chronic hypoxaemic and hypercapnic respiratory failure in hospital and domiciliary settings. This statement also provides practice points in secretion management and palliation in all settings. The statement acknowledges the lack of evidence in many of the above settings and provides research priorities for each of the sections.

Methodology

The Clinical Statement Group (CSG) was chaired by Dr Ingrid du Rand and Dr Murali Shyamsundar. Membership of the CSG was selected through an expression of interest process. The final membership was decided based on a scoring system performed by the chairs independent of each other. The CSG membership is multidisciplinary in nature. The CSG identified key areas requiring clinical practice points. The overall content was developed to reflect the scope approved by the BTS Standards of Care Committee (SOCC). Following discussions of broad statement content, individual sections were drafted by group members. A final edited draft was developed iteratively with feedback from the CSG and reviewed by SOCC. Following SOCC review, the revised statement will undergo public consultation and peer review through the BTS before further revision and final approval.

Section 3: Physiological effects of HFNT

Physiological effects of HFNT

The physiological effects of HFNT are summarised in Table 1. Clinical trials in human subjects as well as bench studies indicate that HFNT confers a range of physiological effects,⁵ summarised in Table 1.

Physiological effect	Clinical impact
Mucociliary clearance	Bench and small clinical studies suggest heated humidification supports mucociliary function and secretion clearance^{6,7}
Dead space washout	- Reduced anatomical dead space in a flow-dependent manner,⁸ with clearance further enhanced by an asymmetrical nasal cannula interface in a benchside study⁹ - Creation of oxygen reservoir where supplementary oxygen is entrained - Carbon dioxide washout
Pulmonary mechanics	- Increases expiratory resistance, mean airway pressure and expiratory time¹⁰ - Improved oxygenation through counteracting peak inspiratory flow rates and reducing entrainment of ambient air¹¹ - Delivery of positive airway pressure that is proportional to flow and dependent on mouth position^{12,13} - Increased end-expiratory lung volume and dynamic compliance in hypoxaemic acute respiratory failure (ARF)¹⁴ - Reduced ventilation inhomogeneity and dead space ventilation - Reduced work of breathing^{14–16}

Table 1: Summary of physiological effects of high flow nasal therapy

Respiratory epithelium functions optimally at core body temperature and 100% relative humidity. The consequence of altered airway conditions is impaired mucociliary function, with altered volume and viscosity of respiratory secretions, reduced ciliary beat frequency and mucus transport velocity, and risk of bronchoconstriction.^{6,17} This increases airway resistance, reduces lung compliance and increases work of breathing, and clinically increases risk of mucus plugging and alveolar decruitment as well as infection. Use of radio-labelled aerosol demonstrates that in patients with Chronic Obstructive Pulmonary Disease (COPD) and bronchiectasis, secretion clearance increases following heating and humidification of inhaled air after 3 hours, which is sustained over 7 days when used as a daily intervention.⁷

HFNT has been shown in patients with acute and chronic respiratory failure to alter pulmonary mechanics. The effects are physiologically different compared to other mechanisms by which respiratory support such as Non-Invasive Ventilation (NIV), Continuous Positive Airway Pressure (CPAP) and Invasive Mechanical Ventilation (IMV) operate, since these use a closed or semi-closed interface/circuit to deliver positive pressure. HFNT is an open-interface system, and the positive airway pressure generated is modest and dependent on total flow and interface leak, including whether the mouth is open or closed. Mean nasopharyngeal pressure

increases with flow: in one study it was approximately 3.3 cmH₂O at 50 L/min with the mouth closed.¹² At very high flows of up to 100 L/min, airway pressure and end-expiratory lung impedance increase progressively with flow.¹³ Higher total flows also reduce ambient-air entrainment and improve the reliability of delivered FiO₂ when they better match or exceed inspiratory demand.¹¹

Introducing flow to the upper airway dilutes and eliminates exhaled gas, thus reducing dead space ventilation. Experimental upper-airway models demonstrate rapid, flow-dependent clearance of exhaled gas from the anatomical dead space during nasal high flow.⁸ Physiological studies in hypoxaemic ARF and COPD demonstrate reductions in respiratory effort and minute ventilation without a corresponding rise in CO₂.^{14,18} Lung model studies demonstrate that application of gas under high flow rates enables continuous flushing of exhaled gas thereby reducing CO₂ rebreathing and can create an oxygen reservoir, which is proportional to flow rate. In stable hypercapnic COPD, variation in prong size did not significantly alter measured respiratory parameters or PaCO₂, although increasing flow increased mean airway pressure and reduced PaCO₂.¹⁹ In bench models, an asymmetrical nasal interface increased anatomical dead-space CO₂ clearance compared with a symmetrical interface.⁹

Invasive measurements of transdiaphragmatic pressure and diaphragm pressure-time product demonstrate that HFNT reduces work of breathing and improves dynamic compliance compared to facemask oxygen in patients with hypoxaemic ARF,¹⁴ and reduces work of breathing and dynamic hyperinflation in COPD patients with chronic hypercapnic respiratory failure albeit to a lesser degree than NIV.^{15,16}

Summary

- HFNT is a non-invasive respiratory therapy that delivers heated humidification to the airways at flow rates of up to 100 L/min depending on device capability.
- Bench and clinical trial data demonstrate that HFNT can optimise respiratory epithelial function with increased ciliary beat frequency and mucus transport velocity observed at 37°C compared to lower temperatures, and improved airway clearance.
- Physiological and bench studies suggest potential benefits of HFNT for mucociliary clearance and of asymmetric nasal interfaces for dead-space washout; however, these findings have not yet been confirmed in clinical trials evaluating patient-important outcomes.
- When total flow adequately matches inspiratory demand, HFNT can provide more reliable delivery of the prescribed FiO₂ than conventional open oxygen systems.
- Lung models demonstrate that continuous flow to the upper airway facilitates dead space washout, through flushing of exhaled gas and creation of an oxygen reservoir.
- HFNT generates modest positive airway pressure that increases with flow and is influenced by interface leak and mouth position.
- Compared to no intervention or face mask oxygen, HFNT reduces work of breathing in patients with acute and chronic respiratory failure.

Section 4: Acute hypoxaemic respiratory failure

Acute hypoxaemic respiratory failure (also termed type 1 respiratory failure) describes the physiological consequence of ventilation-perfusion mismatch, diffusion limitation, right-to-left shunt or reduced inspired oxygen tension.²⁰ These phenomena may arise due to infection, pulmonary oedema, pulmonary embolism and acute exacerbation of airways or parenchymal lung disease. Supplementary oxygen to achieve a target peripheral oxygen saturation (SpO_2) or arterial partial pressure of oxygen (PaO_2) is required to address the physiological derangement whilst disease-specific treatment is instituted.²¹

The aim of oxygen therapy in hypoxaemic ARF is to reduce risk of mortality from hypoxia and reduce the need for intubation with associated complications and mortality. Supplementary oxygen may be delivered at flow rates of up to 5 L/min via conventional nasal cannula or up to 8 L/min via face mask in mild hypoxaemic ARF.²¹ Higher flow rates are provided through venturi masks for FiO_2 of up to 60% at 15 L/min and non-rebreathe masks for $\text{FiO}_2 >60\%$ via 10-15 L/min. Oxygen may be entrained through non-invasive respiratory support therapies including HFNT, NIV and CPAP. IMV may be required where non-invasive oxygen therapy fails. Conventional oxygen therapy (COT) can be defined as oxygen delivered via standard devices such as nasal cannulae, Venturi mask, simple face mask or non-rebreathe mask, excluding HFNT, CPAP, NIV and invasive ventilation.

The main goals of oxygen therapy in this group of patients are to reduce the risk of mortality related to hypoxaemia and to reduce the risk of intubation, which is known to be associated with considerable morbidity. The optimum method of oxygen delivery to achieve these goals is unknown. Many studies have attempted to address this question in patients with hypoxaemic ARF. There is considerable variability between studies in terms of severity of respiratory failure, clinical setting, intervention and outcome.

Physiological effects of HFNT in acute hypoxaemic respiratory failure as compared to COT, NIV and CPAP

Physiological effects: respiratory rate and gas exchange

The evidence synthesis underpinning the 2022 ERS clinical practice guideline found that, compared with COT, HFNT was associated with a significant increase in PaO_2 , with a mean difference of 2.26 kPa, equivalent to 16.7 mmHg, with no significant difference in PaCO_2 . HFNT was also associated with an increase in the $\text{PaO}_2:\text{FiO}_2$ ratio (mean difference 3.33 kPa), although this did not reach statistical significance.²²

A reduction in respiratory rate (RR) was observed with HFNT compared to COT (mean difference -2.25 breaths/min).²² These findings are supported by the SOHO study, which enrolled 1116 patients and demonstrated a reduction in RR in the HFNT group compared with COT. Furthermore, patient-reported outcomes from the SOHO study showed subjective improvement in patient-perceived dyspnoea in 49.5% of patients receiving HFNT compared to 34.6% in the COT group (absolute difference 14.9%).²³

These results are consistent with a Cochrane systematic review of eight randomized controlled trials, which found no significant difference in $\text{PaO}_2:\text{FiO}_2$ ratio after 24 hours between HFNT and COT, but confirmed a modest reduction in RR with HFNT (mean difference -2.02 breaths/min).²⁴

In contrast, when HFNT was compared with NIV or CPAP, meta-analyses demonstrated a lower PaO₂:FiO₂ ratio with HFNT. One analysis reported a mean difference of -7.45 kPa (-58.1 mmHg), while another reported -5.77 kPa (-43.26 mmHg).^{22,24} There was no significant difference in PaCO₂ between HFNT and NIV or CPAP, and either no difference or a small reduction in RR favouring HFNT (mean difference -1.06 breaths/min).²⁴

Summary

- Compared with COT, HFNT is associated with improved oxygenation without consequent CO₂ rise and reduced RR. The reduced RR may be beneficial for minute ventilation if it allows for increased tidal volume.
- NIV or CPAP may lead to improved oxygenation compared to HFNT by recruiting additional alveolar space through positive pressure.

ARF secondary to mixed aetiology: mortality, risk of intubation, comfort and hospital stay

Most large Randomised Controlled Trials (RCTs) evaluating HFNT in ARF typically include patients with mixed causes of respiratory failure, with inclusion determined by severity of hypoxaemia rather than the aetiology of respiratory failure. Of note, community-acquired pneumonia (CAP) was the most common aetiology in the presented evidence base, hence the evidence presented largely relates to CAP.

Mortality

The FLORALI trial compared HFNT with COT and NIV in Intensive Care Unit (ICU) patients with ARF, 64% of whom had pneumonia. The hazard ratio (HR) for death at 90 days, a secondary outcome favoured HFNT compared to both COT (HR 2.01 [95% CI 1.01 to 3.99]) and NIV (HR 2.50 [95% CI 1.31 to 4.78]), acknowledging that NIV is not the standard of clinical care in ARF particularly secondary to pneumonia.²⁵ The SOHO study recruited 1116 patients with hypoxaemic ARF and found no difference in 28-day mortality between HFNT and COT.²³ Pneumonia (including viral pneumonia) was the primary cause of ARF in 88.1% of patients.

Subsequent studies comparing HFNT with COT have not found a difference in mortality.^{26–28} A 2019 systematic review and meta-analysis of 9 RCTs including 2093 patients with ARF concluded there was no mortality difference (relative risk (RR) 0.94 (95% CI 0.67 to 1.31)).²⁹ This conclusion was supported by a further 2020 systematic review and network meta-analysis, which demonstrated no difference in mortality (absolute risk difference -0.04 (95% CrI -0.15 to 0.04)).³⁰ Community acquired pneumonia was the most common cause of ARF in 16 of the 25 included studies in this meta-analysis.

A 2021 meta-analysis including five studies demonstrated no difference in mortality between HFNT and NIV; risk ratio 0.92 (95% CI 0.64 to 1.31).²⁴ More recently, the 2025 RENOVATE multicentre adaptive non-inferiority RCT compared NIV with HFNT in five patient groups. The study included 485 immunocompetent patients with hypoxaemia and demonstrated non-inferiority in terms of the composite primary outcome of intubation or death within 7 days between HFNT and NIV.³¹

Summary

- HFNT does not influence mortality in ARF compared to COT and NIV.

Need for intubation

Avoiding intubation and mechanical ventilation is desirable, both in terms of reducing morbidity, including ventilator-associated pneumonia, and reducing pressure on frequently scarce intensive care resources. A number of studies have compared the effectiveness of HFNT and COT in reducing the need for endotracheal intubation;^{25–28,32,33} a systematic review and meta-analysis concluded HFNT was associated with a reduced risk of intubation compared to COT; relative risk 0.85 (95% CI 0.74 to 0.99).²⁹ A larger meta-analysis which included both patients post-extubation as well as those without prior mechanical ventilation found a stronger treatment effect, although in this case the outcome was defined as treatment failure which included both need for intubation and need for escalation to NIV in those already receiving HFNT; risk ratio 0.62 (95% CI 0.45 to 0.86).²⁴ In both meta-analyses the certainty of evidence was low due to risk of bias and imprecision. The SOHO study demonstrated a reduction in intubation in patients receiving HFNT when compared to COT from 48.4% (268 of 554) in the COT group to 42.4% (236 of 556) in the HFNT group (absolute difference, –5.93 percentage points; 95% CI, –11.78 to –0.08) but the study was not powered to detect a difference in intubation.

In contrast, HFNT has not demonstrated a clear reduction in intubation compared with NIV/CPAP; however, direct comparative evidence remains less extensive than the evidence versus COT.^{24,25,30,31} Although the RENOVATE study used a composite outcome of intubation or death within 7 days, the percentage of patients requiring intubation was similar between HFNT and NIV groups; 31.2% and 29.2% respectively, in keeping with this conclusion.³¹

Summary

- HFNT is likely to reduce the risk of intubation when compared to COT in ARF; there is no significant difference between HFNT and NIV in intubation risk.

Comfort

Patients with severe ARF are frequently tachypnoeic with respiratory distress and comfort is an important factor when deciding upon method of oxygen delivery. The delivery of heated humidified gas via a nasal interface makes HFNT an attractive option in this situation. A comprehensive overview of this comes from a meta-analysis of studies evaluating patient-reported comfort. This concluded HFNT is associated with higher comfort scores compared to NIV, although when compared to COT there is a smaller and more variable effect.²⁴ The certainty of evidence in this meta-analysis for both comparisons was very low.

Summary

- Patient comfort generally favoured HFNT over NIV in a multicentre non-inferiority RCT in patients with hypoxaemia.³¹

Hospital length of stay

Meta-analyses have demonstrated HFNT does not affect hospital length of stay or ICU length of stay compared to COT and NIV.^{24,29,30}

Outcome	HFNT vs COT	HFNT vs NIV/CPAP	Interpretation
Mortality	No consistent mortality benefit demonstrated.	No clear mortality difference compared with NIV/CPAP.	HFNT should not be selected primarily to reduce mortality in mixed-aetiology ARF.
Intubation / treatment failure	HFNT probably reduces intubation or treatment failure compared with COT, although certainty is limited.	HFNT does not clearly reduce intubation compared with NIV/CPAP.	The main benefit of HFNT over COT is reduction in escalation to intubation or higher-level support.
Oxygenation / respiratory rate	HFNT improves oxygenation and reduces respiratory rate in some studies.	NIV/CPAP may improve oxygenation more through positive pressure and alveolar recruitment.	HFNT provides physiological support but less positive-pressure effect than NIV/CPAP.
Comfort / tolerance	Comfort benefit over COT is variable.	HFNT is generally better tolerated than NIV.	Comfort is an advantage, but should not override indications for NIV, CPAP or IMV.
Hospital / ICU length of stay	No consistent reduction.	No consistent reduction.	HFNT should not be expected to reduce hospital or ICU length of stay.

Table 2: Summary of clinical effects of HFNT compared with COT and NIV/CPAP in hypoxaemic ARF of mixed aetiology.

Summary

- In patients with ARF of mixed aetiology, the main benefit of HFNT is in reducing the need for intubation.
- While NIV may be similarly effective in this setting, HFNT is often better tolerated; modality choice should reflect the indication for positive pressure or ventilatory support, clinical trajectory and patient tolerance.
- The benefits of HFNT in patients in whom intubation and ventilation is not considered appropriate are less certain.

Clinical practice points:

- ✓ HFNT may be considered over COT where adequate oxygenation cannot be maintained, but CPAP/NIV may be more appropriate where positive pressure, alveolar recruitment, or ventilatory support is required.

- ✓ HFNT may be considered as an alternative to NIV in selected patients with hypoxaemic ARF where positive-pressure or ventilatory support is not specifically required, taking account of clinical trajectory and patient tolerance.
- ✓ Patient comfort should be considered when selecting respiratory support; however, this should not supersede clinical indications for NIV, CPAP or IMV where these are required.
- ✓ HFNT may be better tolerated than NIV.
- ✓ There is little evidence to support the use of HFNT compared to other methods of oxygen delivery in patients who are not suitable for intubation and ventilation.

Specific clinical conditions: mortality and risk of endotracheal intubation

Immunocompromised patients

Hypoxaemic ARF is the main cause of admission to ICU in immunocompromised patients and the need for intubation and IMV is associated with high mortality rates.^{34–37} Immunocompromised patients are more likely to develop complications such as ventilator-associated pneumonia (VAP).^{34,38} There has therefore been interest in evaluating HFNT in this cohort.

The 2026 SOHO study recruited 1116 patients of which 22.3% of patients were immunocompromised where a prespecified sub-group analysis did not demonstrate a difference in mortality or the rate of intubation.²³ A post-hoc propensity-score analysis of 353 immunocompromised patients with hypoxaemic ARF found no significant reduction in intubation or day-28 mortality with HFNT compared with standard oxygen.³⁹ A larger RCT in 2018 of immunocompromised patients with ARF compared HFNT to COT had a similar conclusion with no difference in mortality as primary outcome or need for intubation as secondary outcome.²⁸ Post-hoc analysis of the FLORALI study also demonstrated no difference in the need for intubation in immunocompromised patients between HFNT and COT.⁴⁰ A retrospective analysis of lung transplant patients with ARF showed a risk reduction for IMV in patients treated with HFNT compared to COT.⁴¹ Systematic review and meta-analysis of the available studies concluded that HFNT reduces the need for intubation and mechanical ventilation in immunocompromised patients compared to COT, although there was no difference in mortality.^{42,43} The reduction in need for intubation in these meta-analyses was driven by a trend favouring HFNT across several studies, and it should be noted that this has not been demonstrated in any RCTs.

For the comparison with NIV, a retrospective observational study suggested a reduced rate of intubation and 28-day mortality for patients treated with HFNT compared to NIV;⁴⁴ a smaller retrospective study suggested similar mortality in patients treated with HFNT and NIV.⁴⁵ The FLORALI-IM RCT randomised 299 immunocompromised patients with ARF to HFNT alone or NIV with a first session of at least 4 hours until clinical improvement and then at least 12 hours per day with additional HFNT.⁴⁶ There was no difference in the primary outcome of 28-day mortality; absolute difference 1.2% (95% CI -9.6 to 11.9) $p = 0.83$ or in the secondary outcome of intubation rate at 28 days.⁴⁶ In the more recent RENOVATE study, non-inferiority between HFNT and NIV for the primary outcome of intubation or death within 7 days was not met in immunocompromised patients with ARF.³¹ The number of patients included in this study was relatively low following early termination of enrolment after an interim analysis.

Summary

- HFNT has not demonstrated a mortality benefit over COT in immunocompromised patients. Meta-analyses suggest a possible modest reduction in intubation compared with COT, although individual RCTs have not consistently demonstrated this effect. Evidence comparing HFNT with NIV remains uncertain.
- Evidence comparing HFNT with NIV in immunocompromised populations remains heterogeneous.

Clinical practice points:

- ✓ HFNT may be considered in immunocompromised patients with hypoxaemic ARF. Current evidence does not demonstrate a mortality benefit, while evidence for reducing intubation compared with COT is inconsistent.

COVID-19 pneumonia and viral pneumonia

Severity of hypoxaemia is a key determinant of disease severity in COVID-19.⁴⁷ Alongside disease-specific therapies, HFNT, CPAP and NIV have all been evaluated as non-invasive respiratory support strategies in COVID-19-related hypoxaemic respiratory failure.

Several RCTs have evaluated the efficacy of HFNT in COVID-19. However, most COVID-19 respiratory support trials were conducted in earlier pandemic waves, before current vaccination, antiviral and immunomodulatory treatment patterns, which may limit applicability to contemporary severe COVID-19.

The HiFLo-COVID trial demonstrated a significant reduction in the need for intubation and a shorter time to clinical recovery, defined as hospital discharge or requirement for no or low-flow conventional oxygen therapy, within 28 days with HFNT compared to COT.⁴⁸

The HENIVOT trial found no difference between NIV and HFNT in the number of days free of respiratory support within 28 days in patients with COVID-19-associated hypoxaemia.⁴⁹

The RECOVERY-RS trial, a parallel-group, adaptive, open-label randomised clinical trial, evaluated CPAP or HFNT compared with COT in patients hospitalised with hypoxaemic ARF secondary to COVID-19. CPAP reduced the composite outcome of tracheal intubation or mortality within 30 days compared to COT (36.3% vs 44.4%; 95% CI -15% to -1%; $P = 0.03$). However, there was no significant difference between HFNT and COT (44.3% vs 45.1%; 95% CI -8% to 6%; $P = 0.83$).⁵⁰ Despite its pragmatic design and low loss to follow-up, the trial was limited by early termination due to declining hospital admissions. Additional limitations included its open-label design, lack of standardisation for escalation to tracheal intubation, longer time to intubation in the CPAP arm (potentially reflecting delayed decision-making or resource factors), and crossover between treatment arms in 17% of participants.

The SOHO-COVID trial reported no difference in 28-day mortality between HFNT and COT (10% vs 11%; $P = 0.60$).⁵¹ Similarly, the COVIDICUS trial found no significant difference in the cumulative incidence of IMV criteria at 28 days between HFNT, CPAP, and standard oxygen strategies.⁵²

The COVID-HIGH trial, the first multicentre RCT evaluating HFNT in hospitalised patients with COVID-19 pneumonia and mild hypoxaemia ($\text{PaO}_2\text{:FiO}_2$ ratio 200–300 mmHg), demonstrated

no significant difference in escalation of respiratory support within 28 days compared to COT. Secondary outcomes—including clinical recovery, time to escalation, ICU admission, and mortality at 28 and 60 days—were also similar between groups.⁵³

A more recent SOHO study (2026) recruited 1116 patients, of whom 53% had viral pneumonia; 87% of these cases (517/592) were attributable to COVID-19. In a predefined subgroup analysis, there was no difference in mortality or intubation rates between HFNT and COT.²³

Systematic reviews and meta-analyses of patients with COVID-19 and hypoxaemic respiratory failure have reported mixed findings. Some demonstrate no difference in mortality or treatment failure between HFNT, COT, and NIV,⁵⁴ while others report reduced 28-day ICU mortality and intubation rates with HFNT compared to COT,⁵⁵ or reduced need for intubation without a mortality benefit.⁵⁶

The RENOVATE trial, a multicentre non-inferiority RCT including 882 patients with COVID-19 and hypoxaemia, demonstrated non-inferiority of HFNT compared to NIV for the primary outcome of intubation or death within 7 days (OR 1.13, 95% CrI 0.94 to 1.38).³¹ There were no significant differences in secondary outcomes, including 28- and 90-day mortality.

The evidence for the use of HFNT in ARF secondary to COVID-19 is summarised in Table S3 (Appendix 1).

Summary

- In patients with COVID-19 and hypoxaemic ARF, HFNT was non-inferior to NIV for intubation or death within 7 days in RENOVATE, while evidence comparing HFNT with COT and CPAP remains mixed.
- HFNT does appear to reduce the need for intubation when compared to COT in ARF secondary to COVID-19.

Clinical practice points:

- ✓ HFNT can safely be used in patients with hypoxaemic ARF secondary to COVID-19. It may be more effective than COT in reducing risk for intubation, but CPAP/NIV are at least as effective and may support oxygen delivery better in some patients.
- ✓ Patient choice and tolerance need consideration when making management decisions to treat hypoxaemic ARF in COVID-19 patients.

Interstitial lung disease

Interstitial lung diseases (ILDs) are a heterogeneous group of diseases characterised by widespread fibrotic and/or inflammatory abnormalities of the lung parenchyma.^{57,58} Respiratory failure is a common complication of advanced ILD or following acute worsening of ILDs and can be classified on the basis of different parameters, including time of onset (acute or chronic), severity (mild to severe), and causes (reversible or irreversible). Patients with ILD also present with acute exacerbations which are associated with a very poor prognosis and are frequently accompanied by an accelerated decline in lung function. These exacerbations are thought to be either idiopathic or precipitated by acute events such as infection, aspiration, surgery and heart failure.⁵⁹ Whilst acute exacerbations have thus far been

most widely studied within the IPF group of ILD, they are becoming increasingly recognised as a complication of other fibrosing ILD.

Management of ARF in ILD frequently presents a clinical and ethical challenge, given the lack of benefit of IMV in the majority of patients and poor overall prognosis.⁶⁰ The decision to start non-invasive respiratory support is complex and is determined by a number of factors, including the nature of the underlying ILD and the acute insult leading to ARF. Either way, there is a high risk of mortality in this group and patients with advanced ILD should receive appropriate counselling about the prognosis of the disease and early palliative care input. Due consideration should be given to formulation of a weaning plan if the patient transitions to palliative care.

Oxygen therapy is the mainstay of supportive treatment of acute respiratory failure in ILD. The evidence for HFNT in this context is limited; a retrospective analysis demonstrated HFNT had a survival rate equivalent to NIV and was better tolerated by patients with ARF in ILD who had a do not resuscitate order and who were not for ICU admission.⁶¹ HFNT in this setting can enable oral intake and the ability to communicate when deteriorating towards death, suggesting that HFNT may be a reasonable palliative intervention alongside clearly communicated boundaries of its role and planning for withdrawal. A small retrospective cohort analysis of 17 patients with AE-IPF showed implementation of a treatment algorithm incorporating HFNT led to a lower-than-expected short term mortality.⁶² A recent systematic and narrative synthesis showed that HFNT as compared to NIV as a support for ARF was more comfortable and better tolerated with no clear difference in mortality.⁶³

Summary

- There is limited evidence to support the use of HFNT in ILD related ARF.
- HFNT appears to be well tolerated and may have a role with palliative intent to support oxygenation and allow time for discussion with patients and families as well as optimisation of symptom control.

Clinical practice points:

- ✓ HFNT may be considered on an individualised basis in ILD-related hypoxaemic ARF where a potentially reversible contributor is being treated, recognising the limited evidence of clinical benefit and poor prognosis, particularly in advanced fibrotic disease.
- ✓ HFNT may support palliative care in patients with ILD-related hypoxaemic ARF by improving symptom control, facilitating communication, and allowing time for patient/family discussions.
- ✓ Institution of HFNT in patients with ILD should include a weaning plan for respiratory support, developed with palliative care input.

Cardiogenic pulmonary oedema

International guidelines recommend the use of CPAP and NIV in acute heart failure in patients with respiratory distress to improve gas exchange and reduce the risk of endotracheal

intubation.⁶⁴ A previous meta-analysis has demonstrated a reduction in mortality and need for intubation when CPAP was used compared to COT.⁶⁵ The use of HFNT is associated with the generation of a small amount of positive end expiratory pressure, and there has been interest as to whether this may translate into clinical benefits for patients with cardiogenic pulmonary oedema.^{12,66} In an emergency-department RCT of 128 patients with cardiogenic pulmonary oedema, HFNT improved early respiratory distress/physiological parameters compared with conventional oxygen.²⁷

A systematic review and meta-analysis of 16 studies comparing HFNT, COT and NIV or CPAP in patients with acute heart failure was performed in 2023.⁶⁷ This demonstrated a reduction in rate of intubation for HFNT compared to COT; odds ratio 0.29 (95% CI 0.14 to 0.58), although there was no difference between HFNT and NIV or CPAP. There was also a reduction in respiratory rate and improvement in oxygenation with HFNT compared to COT, with no difference between HFNT and NIV or CPAP.⁶⁷

The RENOVATE multicentre non-inferiority RCT compared NIV and HFNT in 272 patients with acute cardiogenic pulmonary oedema. Non-inferiority for the primary outcome of intubation or death within 7 days was met, with no difference in the secondary outcomes of 28- and 90-day mortality.³¹ Of note, patients who required NIV prior to randomisation were excluded, potentially limiting the generalisability.

Summary

- HFNT demonstrated lower intubation rates, reduced respiratory rate, and improved oxygenation in patients with acute cardiogenic pulmonary oedema when compared to COT.
- There is insufficient evidence to recommend HFNT, CPAP or NIV as the preferred modality in acute cardiogenic pulmonary oedema.

Clinical practice points:

- ✓ HFNT should be considered over COT to treat ARF in patients with acute cardiogenic pulmonary oedema to reduce work of breathing, improve oxygenation and reduce risk of intubation.
- ✓ No clear superiority of HFNT over CPAP/NIV has been established.
- ✓ HFNT in patients with cardiogenic pulmonary oedema should be delivered in a critical care setting or a high monitoring area such as a coronary care unit.

Asthma

Asthma is the most common chronic respiratory disease and is characterised by airway hyperresponsiveness and reversible airflow obstruction.^{68–71} An episode of acute exacerbation results in expiratory airflow obstruction due to airway inflammation, bronchospasm and mucus hypersecretion.^{70,72}

Three RCTs have demonstrated HFNT may reduce dyspnoea compared to COT, but with no difference in PaCO₂, PaO₂, intubation or hospital length of stay. The trials were small, with HFNT flow rates ranging from 15–40 L/min, and the certainty of evidence therefore remains

limited.^{73–75} Larger adequately powered RCTs are required to clarify the role of HFNT in acute asthma.

The possibility of nebulising drugs via HFNT represents a potential additional treatment feature, allowing the administration of inhaled bronchodilation therapy uninterrupted with concomitant oxygen therapy.⁷⁶ The safety and efficacy of delivering inhaled therapy in this way still need to be assessed with RCTs. There are concerns about the potential increased upper airway drug deposition and drug dilution in the anatomical dead space, affecting drug delivery in clinical practice. Reducing the HFNT flow rate will improve aerosol delivery within the lungs but might reduce respiratory support.⁷⁷ Larger RCTs are needed to clarify the role of HFNT in severe asthma exacerbations.

Summary

- HFNT is well tolerated in asthmatic patients with ARF due to acute asthma exacerbations but should only be considered in a critical care setting.
- There is insufficient evidence to recommend bronchodilation therapy via HFNT or that HFNT reduces intubation or mortality in this group of patients.

Clinical practice points:

- ✓ HFNT has not demonstrated an improvement in oxygenation, risk of IMV or hospital LOS compared with COT, but limited evidence from small trials suggests possible improvement in dyspnoea.
- ✓ If non-invasive respiratory support is applied in acute asthma, this should only be undertaken in a critical care environment to monitor for treatment failure and to enable rapid endotracheal intubation.

Pulmonary embolism

Venous thromboembolism (VTE), clinically presenting as deep vein thrombosis (DVT) and/or pulmonary embolism (PE), is globally the third most frequent cause of acute cardiovascular syndrome behind myocardial infarction and stroke.⁷⁸ Right ventricular (RV) failure due to acute pressure overload is considered the primary cause of death in severe PE. Severe respiratory failure in PE is predominantly a consequence of haemodynamic disturbances,⁷⁹ although milder hypoxaemia is commonly observed and is mostly due to ventilation perfusion mismatch.

There are a small number of studies specifically evaluating the use of HFNT in acute PE. In a retrospective case series of 17 patients admitted to ICU with ARF due to acute PE, HFNT improved oxygenation and respiratory rate within two hours of transitioning from low-flow oxygen to HFNT.⁸⁰ In a small comparative study with early end points of 58 patients in ICU with acute PE, HFNT led to an improvement in oxygenation and respiratory rate compared with COT.⁸¹

Summary

- HFNT may improve oxygenation and reduce respiratory rate in hypoxaemic ARF due to acute pulmonary embolism, although evidence is limited to small ICU studies.

Clinical practice points:

- ✓ HFNT could be considered to treat hypoxaemic ARF in patients with acute PE to reduce respiratory rate and work of breathing and improve oxygenation.
- ✓ HFNT in patients with acute PE should be delivered in a critical care setting or a high monitoring area.

Bronchiectasis

Bronchiectasis is characterised by chronic airway dilatation with recurrent exacerbations, which may be infective, inflammatory, viral, or of uncertain trigger.⁸²

ARF is a common cause of death in patients with bronchiectasis.⁸³ HFNT has emerged as a promising intervention,²² offering both clinical and physiological benefits including alveolar recruitment, dead space washout,⁸⁴ and airway clearance,⁸⁵ and is well tolerated by patients.⁸⁶

A single-centre feasibility study, without a control arm, evaluating the effects of HFNT in 15 patients with exacerbations of COPD with bronchiectasis identified that HFNT improved dyspnoea score, RR, gas exchange, and increased mucus clearance.⁸⁵ A randomised crossover physiological study comparing HFNT with NIV in patients with cystic fibrosis found that HFNT and NIV have similar effects on diaphragmatic work, but HFNT conferred additional physiological benefits by decreasing RR and Minute Ventilation.⁸⁷

Summary

- HFNT may improve dyspnoea, comfort, RR and mucus production in patients with acute exacerbation of bronchiectasis, but the evidence is based on small clinical studies.

Clinical practice points:

- ✓ HFNT may be considered as an adjunct in selected patients with bronchiectasis exacerbations and ARF where oxygenation, comfort or secretion clearance are problematic; however, evidence is indirect and limited.

Section 5: Acute hypercapnic respiratory failure

Acute Hypercapnic Respiratory Failure (AHRF) reflects ventilatory failure due to increased physiological load relative to respiratory muscle capacity. The most common causes are COPD exacerbations, obesity hypoventilation syndrome, and neuromuscular disease.⁸⁸

NIV remains the established first-line ventilatory support for AHRF, with strong evidence demonstrating reductions in mortality and intubation rates in COPD.⁸⁹ NIV is also effective in obesity-related ventilatory failure and is considered standard of care in acute acidaemic hypercapnia.⁸⁸

HFNT is increasingly used as an alternative or adjunctive respiratory support modality despite limited high-certainty evidence in hypercapnic disease states. It delivers heated humidified gas at high flow rates, generating washout of anatomical dead space and mild positive airway pressure, lowering arterial CO₂.¹

A retrospective study demonstrated that HFNT used as initial respiratory support in hypercapnic patients was associated with reductions in PaCO₂ within 24 hours, with higher APACHE II scores predicting treatment failure.⁹⁰

Physiological studies demonstrate favourable changes in respiratory mechanics and reduced work of breathing, although the magnitude of effect is substantially less than NIV, which offers inspiratory support and thus greater direct ventilatory assistance in established AHRF.^{15,16,88} For this reason, HFNT should not be considered a substitute for NIV in patients with acidaemic AHRF, or in patients with ventilatory pump failure due to neuromuscular disease, chest wall disease, severe obesity-related respiratory failure, or other conditions where NIV is clinically indicated.

HFNT compared to COT: clinical effects

Several randomised controlled trials and meta-analyses have evaluated HFNT in acute COPD-related hypercapnic respiratory failure compared with conventional oxygen therapy.

Li et al. demonstrated reduced treatment failure (defined as escalation to NIV or intubation) in patients with acute compensated hypercapnia treated with HFNT compared with COT.⁹¹ However, this study excluded acidaemic patients, limiting generalisability.

In contrast, Xia et al. conducted a multicentre RCT in mild hypercapnic COPD exacerbations and found no significant reduction in intubation criteria or progression to NIV with HFNT compared with COT in acute exacerbations of COPD (AECOPD) with mild hypercapnia (pH ≥ 7.35).⁹²

Physiological crossover data from Pilcher et al. demonstrated reductions in transcutaneous CO₂ with HFNT without changes in RR or oxygen saturation.⁹³

Systematic reviews suggest small physiological improvements in gas exchange but highlight significant heterogeneity and low certainty of evidence across trials.⁹⁴

Observational evidence also suggests that HFNT may be feasible as rescue respiratory support in selected patients with moderate hypercapnic respiratory failure who cannot tolerate or have contraindications to NIV, but treatment failure and need for intubation remain important concerns.⁹⁵

Summary

- Evidence for HFNT over COT in AHRF is limited and inconsistent; it should not be extrapolated to acidaemic or non-COPD ventilatory failure.
- HFNT may provide modest physiological benefit in mild AHRF without acidaemia, but there is inconsistent evidence for reduction in treatment failure or escalation to ventilatory support.

Clinical practice points:

- ✓ NIV remains first-line for treatment of acidaemic AHRF.
- ✓ HFNT should not be routinely used in patients with compensated AHRF to prevent progression of hypercapnia.
- ✓ HFNT may be considered in selected patients with mild COPD-related AHRF, particularly where controlled oxygen delivery is required and there is no acidaemia.
- ✓ HFNT should not delay escalation to NIV where NIV is clinically indicated, particularly in patients with pH <7.35, worsening acidaemia, rising PaCO₂, increasing work of breathing or clinical deterioration.
- ✓ HFNT is not recommended as primary ventilatory support for AHRF due to neuromuscular disease, chest wall disease, severe obesity-related respiratory failure, or other causes of ventilatory failure where NIV is indicated.
- ✓ Patients should be managed with target oxygen saturations of 88–92% in known or suspected hypercapnia.^{21,88}
- ✓ Early reassessment (within 1–2 hours) is essential to identify non-responders.
- ✓ HFNT use in hypercapnia should only occur with a clear escalation plan specifying when NIV or IMV should be instituted, where appropriate.
- ✓ Patients receiving HFNT should be closely monitored for rising PaCO₂, respiratory fatigue, or progression of acidaemia.

HFNT compared to NIV: clinical effects

NIV remains the gold-standard treatment for acidaemic AHRF.

Direct comparisons of HFNT and NIV in AHRF have produced heterogeneous physiological results,^{96–100} but NIV provides established pressure support and remains the standard intervention for acidaemic AHRF.^{88,101} Di Mussi et al. showed reduced neuroventilatory drive and work of breathing with HFNT post-extubation, but without equivalent ventilatory correction compared with NIV.¹⁶

A more recent randomised study comparing HFNT at 30 or 50 L/min with NIV also demonstrated short-term blood-gas improvement across treatment groups, although it was not designed to establish superiority for major clinical outcomes.¹⁰²

Cortegiani et al. performed a multicentre non-inferiority RCT in COPD exacerbation and found HFNT non-inferior to NIV for short-term PaCO₂ reduction at 2 hours using the prespecified

non-inferiority margin; however, 32% of patients initially receiving HFNT required NIV by 6 hours, and one required IMV.¹⁰³

Pantazopoulos et al. reported numerically higher treatment failure with HFNT (19.6% vs 14.8%) without a statistically significant difference. HFNT was associated with lower dyspnoea and discomfort, although the study was underpowered.¹⁰⁴

Tan et al. conducted a larger multicentre trial and reported significantly higher treatment failure and intubation rates with HFNT compared with NIV in patients with mild-to-moderate acidaemia.¹⁰⁵

Systematic reviews confirm inconsistent results but overall trend toward superior ventilatory efficacy of NIV, particularly in acidaemic patients.^{101,106}

Summary

- The current evidence comparing HFNT vs NIV indicates HFNT does not reliably correct hypercapnia or acidaemia: although some trials show similar short-term physiological outcomes, treatment failure may be more frequent with HFNT in acidaemic AECOPD, and NIV should remain first-line therapy.

Clinical practice points:

- ✓ NIV should remain first-line therapy for AHRF with acidaemia (pH <7.35).
- ✓ HFNT should not be used as a replacement for NIV in acidaemic AHRF.
- ✓ HFNT may be considered where NIV is not tolerated or is contraindicated, but supporting clinical evidence is limited and low certainty.
- ✓ In patients with acidaemic AHRF who remain eligible for IMV, HFNT should only be considered where NIV is not tolerated or cannot be delivered. This should be delivered in a critical care setting with close monitoring and immediate access to intubation, as HFNT must not delay IMV where clinically indicated.

HFNT during planned NIV breaks

HFNT has been evaluated as a bridging strategy during NIV interruptions, aiming to maintain oxygenation, improve comfort and reduce interface-related complications.

Spoletini et al. demonstrated improved comfort and reduced eye irritation when HFNT was used during NIV breaks, although the study was underpowered for clinical outcomes.¹⁰⁷

Longhini et al. demonstrated physiological stability during HFNT use following NIV interruption in hypercapnic patients, with no deterioration in gas exchange compared with oxygen therapy.¹⁰⁸

However, there is no high-quality evidence demonstrating improved survival or reduced intubation rates with this strategy.

Summary

- HFNT may improve patient comfort during NIV breaks but has no proven clinical outcome advantage.

Clinical practice points:

- ✓ Based on limited evidence, HFNT may be considered on an individualised basis during planned NIV breaks to improve comfort and tolerance, while maintaining oxygenation and supporting CO₂ washout.
- ✓ HFNT should not replace NIV unless there is clear intolerance or contraindication.
- ✓ NIV should be restarted promptly if hypercapnia worsens during HFNT use on blood gas or transcutaneous CO₂ monitoring, or if work of breathing increases.

HFNT compared with COT and NIV: comfort, tolerance, and patient experience

Delivering oxygen via HFNT is recommended under physiological conditions (flow rate that matches patient effort, core body temperature, 100% relative humidity). However, patient tolerance of these settings is variable.

HFNT is generally better tolerated than NIV due to avoidance of mask interfaces, with improved comfort and reduced skin breakdown reported in multiple RCTs.^{104–106} However, comfort outcomes are inconsistent across studies due to variability in scoring systems and study design.

Survey data indicate widespread HFNT use in COPD-related AHRF despite limited high-certainty evidence.³

Variability in flow settings, temperature titration, and patient adaptation likely contributes to heterogeneity in reported outcomes.

D'Cruz et al. demonstrated that HFNT settings often require down-titration during recovery from COPD exacerbations, highlighting the dynamic nature of patient demand and tolerance.¹⁰⁹

Summary

- There is conflicting evidence for the ability of HFNT to improve comfort, tolerability and dyspnoea when compared to COT. HFNT use cannot be recommended for this purpose over COT in patients with AHRF.
- HFNT is better tolerated than NIV in many patients but does not consistently improve physiological or clinical outcomes.

Clinical practice points:

- ✓ HFNT settings should be individualised and titrated to patient comfort and work of breathing.
- ✓ Flow rates ≥30 L/min should generally be used to achieve physiological effect.

- 1021 ✓ Temperature and humidity settings may require adjustment during treatment and
- 1022 recovery according to patient tolerance and secretion burden.
- 1023 ✓ Comfort should not supersede clinical indications for NIV when required.

Consultation draft

Section 6: Practical aspects of managing HFNT in patients with acute respiratory failure

Practical aspects of acute respiratory failure

HFNT is increasingly used in ARF across emergency departments, respiratory wards, respiratory support units and critical care settings. Despite its physiological benefits and increasing clinical familiarity, HFNT remains a support modality associated with significant disease severity and high short-term mortality in real-world cohorts.

Unlike NIV, HFNT has no universally mandated governance framework, resulting in wide variability in monitoring, staffing, escalation planning, competency requirements, and location of care. This section addresses mortality risk, appropriate clinical environment, monitoring standards, escalation pathways, and governance principles for safe HFNT delivery.

Real-world use of HFNT is widespread across acute hospital settings, including outside critical care environments, despite limited high-certainty evidence, and variable governance structures and monitoring. An international survey of 1176 clinicians demonstrated frequent use of HFNT in ARF and in AECOPD with AHRF, highlighting significant heterogeneity in practice and supporting the need for standardised guidance.^{3,4}

Mortality rates

Although HFNT may improve outcomes in selected acute settings, patients requiring HFNT often have severe ARF and are therefore at high risk of mortality. HFNT is frequently used in patients with severe hypoxaemia or mixed respiratory failure, and mortality rates reflect underlying disease severity rather than device-related harm.

Reported mortality varies widely according to underlying diagnosis, treatment limitations and care setting. In a recent five-hospital retrospective cohort, 24.5% of HFNT episodes were followed by intubation and 29.3% by death or discharge to hospice.¹¹⁰ Mortality is highest in patients with advanced ILD or do-not-intubate status, and lower in mixed ARF cohorts. Emergency department and RSU cohorts also demonstrate substantial mortality, reinforcing that HFNT use is usually a marker of high acuity rather than low-risk oxygen supplementation.^{26,27,100}

Across studies, HFNT use is consistently associated with moderate-to-high mortality reflecting advanced respiratory failure, reinforcing its role as a treatment for high-acuity patients rather than low-risk oxygen supplementation.

A large multi-hospital retrospective cohort study by Bouhassira et al. examined real-world HFNT use across heterogeneous acute respiratory failure populations.¹¹⁰ The study confirmed that HFNT is predominantly used in patients with high illness severity and demonstrated substantial variability in outcomes depending on underlying diagnosis, escalation decisions, and location of care. Mortality remained significant across cohorts and was strongly associated with treatment limitation decisions, baseline hypoxaemia, and failure to escalate to ventilatory support when required. This reinforces that HFNT use is best interpreted as a marker of advanced respiratory failure rather than a therapy associated with intrinsic mortality risk.¹¹⁰

1065 **Monitoring and location of use**

1066 The physiological severity of patients receiving HFNT is often comparable to those triggering
1067 high NEWS2 scores.

1068 Patients with NEWS2 ≥ 5 :

- 1069 • represent a threshold for urgent clinical review and enhanced monitoring¹¹¹
- 1070 • require at least hourly observations¹¹¹
- 1071 • warrant continuous monitoring and emergency clinical response once NEWS2 ≥ 7 ¹¹¹

1072 In comparison, HFNT cohorts frequently demonstrate:

- 1073 • high FiO₂ requirements (often ≥ 0.6 –1.0)
- 1074 • significant baseline hypoxaemia
- 1075 • frequent escalation to NIV or intubation

1076 Despite this, HFNT is often delivered in ward environments, including surgical and general
1077 medical wards.

1078 A UK/North American survey reported HFNT use in non-respiratory ward environments in
1079 >25% of cases, including surgical wards.³

1080 The BTS Respiratory Support Unit (RSU) audit identified:

- 1081 • that at least 40% of patients receiving acute high-flow therapy were managed in
1082 general ward environments with unenhanced staffing¹¹²
- 1083 • lower mortality among high-risk patients managed in enhanced respiratory-care
1084 settings, although these observational data cannot establish a causal effect of location
1085 of care¹¹²

1086 A recommendation from the BTS RSU audit was that:

1087 *“Acute respiratory support (NIV, HFNT, CPAP) for patients with acute lung disease should be*
1088 *delivered in an RSU or equivalent area with appropriate staffing levels (including HDU and*
1089 *critical care areas) and should not be used routinely in unenhanced, standard ward areas.”¹¹²*

1090 Unlike HFNT, NIV:

- 1091 • is restricted to designated clinical areas¹¹³
- 1092 • requires trained staff and escalation pathways¹¹³
- 1093 • has mandated monitoring standards and audit frameworks¹¹³

1094 There is strong evidence that NIV outcomes improve in specialist RSUs compared with
1095 general wards.¹¹² HFNT, although less invasive, is now used in comparable severity
1096 populations, supporting similar governance expectations.¹¹⁴

1097 In patients receiving HFNT with symptom-focused intent, monitoring should prioritise comfort
1098 and symptom burden rather than physiological targets (see Section 10).

1099

1100 **Objective assessment of HFNT response**

1101 The ROX index (Respiratory Rate-Oxygenation index), calculated as $(\text{SpO}_2/\text{FiO}_2) \div$
1102 respiratory rate, may be used as an adjunctive bedside tool to support early recognition of
1103 HFNT failure in hypoxaemic ARF. In patients with pneumonia-associated hypoxaemic ARF,
1104 the ROX index may support early identification of HFNT success or failure, with lower values
1105 and falling serial values associated with higher risk of treatment failure. Original validation
1106 work identified ROX values below 2.85, 3.47 and 3.85 at 2, 6 and 12 hours respectively as
1107 predictors of HFNT failure, with ROX >4.88 as reassuring for likely success and ROX <3.85
1108 as high risk for failure.¹¹⁵

1109 ROX should not be used in isolation or as a substitute for clinical judgement. Escalation
1110 decisions must also consider work of breathing, trajectory of oxygen requirement, mental
1111 status, haemodynamic stability, arterial blood gases, underlying diagnosis, the agreed
1112 treatment escalation plan, and patient preference. A falling ROX across serial measurements
1113 should prompt urgent senior review even if the absolute value has not crossed a predefined
1114 threshold.

1115

1116 **Escalation**

1117 HFNT is associated with substantial rates of escalation to NIV, IMV, or death, particularly in
1118 ARF cohorts.

1119 Given this, HFNT should be treated similarly to NIV regarding:

- 1120 • treatment limitation decisions
- 1121 • escalation planning
- 1122 • senior clinician involvement

1123 NIV guidelines require early documented treatment escalation plans due to high failure rates
1124 in AHRF.^{88,113} Given the acuity and failure risk associated with HFNT, the same governance
1125 principle is appropriate for acute HFNT.

1126 Failure to recognise HFNT non-response may delay escalation to life-saving ventilation.¹¹⁶

1127

1128 **Governance**

1129 Multiple UK, European, and international surveys demonstrate:^{3,4}

- 1130 • lack of HFNT protocols
- 1131 • limited audit structures
- 1132 • variability in escalation thresholds
- 1133 • inconsistent training requirements

1134 This contrasts sharply with NIV,^{113,114} which is supported by:

- 1135 • national guidelines
- 1136 • mandatory documentation standards
- 1137 • RSU governance frameworks

- 1138 • structured competency training

1139 The BTS RSU framework recommends that acute respiratory support (including HFNT) should
1140 be delivered in RSU or equivalent areas with appropriate staffing and monitoring and not in
1141 standard unenhanced wards.¹¹⁴

1142 An example local protocol covering the initiation, monitoring, escalation and weaning is
1143 provided in Appendix 2. Suggested indications for HFNT across different respiratory failure
1144 phenotypes are summarised in Appendix 3. A standalone HFNT management and
1145 reassessment flowchart for hypoxaemic ARF is provided in Appendix 6 for quick reference.
1146 These resources should be adapted to local escalation, monitoring and governance pathways.

1147 HFNT should not delay urgent intubation, NIV or CPAP where these are clinically indicated.
1148 Particular caution is required in patients with inability to protect the airway, severe or
1149 worsening acidaemia, rapidly rising PaCO₂, severe respiratory muscle fatigue, haemodynamic
1150 instability, untreated pneumothorax, facial or nasal trauma preventing safe interface use, or
1151 where adequate monitoring and escalation cannot be provided.

1152 **Summary**

- 1153 ➤ HFNT is predominantly used in moderate–severe acute respiratory failure, with
1154 mortality reflecting underlying disease severity rather than device effect.
- 1155 ➤ Mortality and escalation rates vary substantially depending on:
 - 1156 • diagnosis (e.g. ILD, pneumonia, COVID-19)
 - 1157 • treatment limitation decisions
 - 1158 • escalation to ventilatory support
- 1159 ➤ HFNT is commonly used in high-acuity patients outside critical care environments,
1160 including general wards.
- 1161 ➤ International survey data show widespread HFNT use with major variability in
1162 indications, settings, and escalation thresholds.
- 1163 ➤ HFNT use is frequently associated with subsequent escalation to NIV, intubation, or
1164 death, reflecting severity of illness rather than treatment efficacy.
- 1165 ➤ Outcomes appear to be influenced by location of care and escalation practices, with
1166 better outcomes reported in structured respiratory support environments.
- 1167 ➤ HFNT requires standardised failure criteria, monitoring requirements, escalation
1168 pathways and governance structures.
- 1169 ➤ Compared with NIV, HFNT has no proven equivalent efficacy in ventilatory failure and
1170 no established mortality benefit in AHRF.

1171

1172 **Clinical practice points:**

- 1173 ✓ HFNT is a high-risk therapy indicative of severe acute respiratory failure.
- 1174 ✓ Early senior clinical review should occur in all patients initiated on HFNT.
- 1175 ✓ HFNT should be delivered in enhanced monitoring environments such as RSU, HDU,
1176 ICU, coronary care or equivalent areas with trained staff and escalation pathways.

- 1177 ✓ Delivery in standard unenhanced ward environments without adequate monitoring,
1178 trained staff and escalation pathways is not appropriate for patients with significant
1179 oxygen requirements or clinical instability.
- 1180 ✓ The BTS/ICS RSU guidance specifically states that the minimum ratio recommended
1181 for an RSU is 1:4, with more staff required as acuity increases.¹¹⁴
- 1182 ✓ HFNT must only be initiated with a documented escalation plan agreed by a senior
1183 clinician (ST3+/respiratory or critical care equivalent).
- 1184 ✓ Escalation plans should define:
- 1185 ● suitability for NIV
 - 1186 ● suitability for IMV
 - 1187 ● any agreed limits to treatment escalation, where appropriate
 - 1188 ● palliative care strategy and weaning or withdrawal plan where NIV or IMV is
1189 not appropriate
- 1190 ✓ Failure to respond should prompt early senior review, with timely escalation of
1191 respiratory support or transition to symptom-focused palliative care in accordance with
1192 the agreed treatment escalation plan.
- 1193 ✓ Local HFNT protocols should include objective reassessment criteria, such as serial
1194 ROX index measurement in hypoxaemic ARF, alongside clinical assessment of work
1195 of breathing, oxygen requirement, gas exchange and mental status.
- 1196 ✓ All institutions using HFNT should maintain a formal HFNT policy, including:
- 1197 ● indications and contraindications
 - 1198 ● initiation pathway or flowchart
 - 1199 ● initiation protocols
 - 1200 ● monitoring requirements
 - 1201 ● definition of HFNT failure
 - 1202 ● escalation and ceiling-of-care pathways
 - 1203 ● weaning strategies
- 1204 ✓ HFNT use should be evaluated in routine audit and morbidity/mortality review
1205 processes.
- 1206 ✓ Staff delivering HFNT must demonstrate documented competency-based training.
- 1207 ✓ HFNT should be integrated into structured acute respiratory failure pathways, not used
1208 as an isolated therapy.
- 1209 ✓ Oxygen infrastructure must support safe delivery of multiple high-flow devices where
1210 used at scale.
- 1211 ✓ HFNT should not delay escalation to ventilatory support such as NIV or IMV when
1212 clinically indicated.

Section 7: Domiciliary HFNT in chronic respiratory failure

The impact of HFNT on physiological, clinical and patient-reported outcomes in chronic hypoxaemic respiratory failure

In patients with COPD, home HFNT may reduce exacerbation frequency and breathlessness, and improve health-related quality of life (HRQoL) in stable hypoxaemic COPD patients, when used as an adjunct to long-term oxygen therapy (LTOT).¹¹⁷ Studies conducted independently of, and during, pulmonary rehabilitation programmes indicate improved exercise endurance when used during physical activity in this population.^{118–120} Mechanisms of action, and optimal duration of use or settings inclusive of flow rate or temperature have not been fully established.

There is little evidence exploring its use as an oxygen delivery tool in non-COPD populations with hypoxaemic respiratory failure.

Safe implementation of domiciliary HFNT requires clearly defined clinical management plans, appropriate equipment provision and electrical supply prior to initiation. Interruptions to therapy, including those required for routine device maintenance or resulting from electrical failure, may lead to periods of inadequate oxygenation without adequate backup oxygen delivery systems. Patient education and appropriate management plans are therefore essential to ensure safe continuity of care in the community setting. Treatment burden should be considered when selecting patients for domiciliary HFNT with practical considerations made in relation to device adherence, power dependency, and provision of alternative oxygen delivery during device interruption (see Section 8).¹²¹

Long-term home HFNT has been evaluated predominantly in COPD and bronchiectasis, with a smaller evidence base in ILD.¹²¹ A systematic review of long-term home HFNT (≥4 weeks) use (n = 701) reported reductions in exacerbations and improvements in quality of life compared to usual care or respiratory therapies, with good adherence and safety profile, but was limited by variable study quality and heterogeneity.¹²¹

Chronic hypoxaemic respiratory failure

Chronic hypoxaemic respiratory failure arises from mechanisms including ventilation–perfusion mismatch, diffusion limitation, right-to-left shunt, and reduced inspired oxygen tension. LTOT is recommended in appropriately selected patients to improve survival and reduce symptom burden.¹²²

HFNT has been evaluated as an oxygen delivery modality in the domiciliary setting, primarily as an adjunct to LTOT. The current evidence base is largely derived from studies in patients with COPD, with limited data available in other causes of chronic hypoxaemic respiratory failure.

Chronic obstructive pulmonary disease

In a randomised crossover physiological study, Fraser et al. compared HFNT delivered at 30 L/min with entrained oxygen to low-flow oxygen (2–4 L/min via nasal cannula) in stable COPD patients receiving LTOT.¹²³ HFNT maintained comparable SpO₂ while reducing respiratory rate and transcutaneous CO₂ and increasing tidal and end-expiratory lung volumes.

Storgaard et al. conducted a 12-month randomised controlled trial evaluating 200 patients with stable hypoxaemic COPD.¹¹⁷ HFNT (20 L/min with entrained oxygen) used for a mean of approximately 6 hours/day reduced exacerbation frequency and improved dyspnoea, HRQoL and exercise capacity. Hospital admission rates were also lower in modelling related to treatment exposure, while all-cause mortality did not differ.

An economic evaluation based on the Danish Storgaard cohort estimated an ICER of £3,605 per quality-adjusted life year (QALY), with an 83–92% probability of cost-effectiveness at thresholds of £20,000–£30,000/QALY.¹²⁴

A feasibility RCT has also explored home HFNT during recovery from severe COPD exacerbation, demonstrating feasibility and acceptability but not providing definitive efficacy evidence.¹⁰⁹

Evidence for HFNT during pulmonary rehabilitation remains limited and heterogeneous. A systematic review demonstrated no consistent improvement in exercise capacity, dyspnoea or HRQoL compared with conventional oxygen therapy.¹²⁰

Bronchiectasis

Evidence for domiciliary HFNT in bronchiectasis is limited and largely derived from observational and mixed-population studies.

In a mixed COPD/bronchiectasis RCT, long-term humidified high-flow therapy reduced exacerbation days and prolonged time to first exacerbation compared with usual care.¹²⁵

In a matched retrospective case-control study in patients with bronchiectasis, Crimi et al. found fewer exacerbations and hospitalisations with long-term HFNT, alongside small improvements in pulmonary function.¹²⁶ A subsequent single-arm long-term crossover study by Simioli et al. similarly reported reductions in exacerbations and hospitalisations without significant improvement in spirometric lung function.¹²⁷

Interstitial lung disease

Evidence for HFNT in ILD is limited to small pilot and observational studies.

In a small heterogeneous ILD cohort (n=9), HFNT use over six weeks was associated with improvements in dyspnoea and exercise capacity.¹²⁸

Exercise crossover trials have produced mixed results. Harada et al. demonstrated improved endurance time with HFNT compared with Venturi-mask oxygen in IPF, whereas Suzuki et al. found no significant overall difference in fibrotic ILD, although a responder subgroup appeared to benefit.^{129,130}

Summary

- Current evidence is strongest in COPD but limited elsewhere, and indicates that home HFNT, when used as an adjunct to LTOT in selected patients with stable COPD and chronic hypoxaemic respiratory failure, may reduce exacerbation frequency and improve symptoms, HRQoL and exercise capacity.

1294 ➤ Based on limited and mostly observational evidence, home HFNT may reduce
1295 exacerbation frequency and improve symptoms or airway clearance in selected
1296 patients with bronchiectasis.

1297 ➤ In patients with ILD and hypoxaemic respiratory failure, HFNT may improve exercise
1298 tolerance and capacity, although evidence is limited to small studies and short-term
1299 physiological or exercise outcomes.

1300

1301 ***Clinical practice points:***

1302 ✓ Home HFNT may be considered as an adjunct to LTOT in selected patients with stable
1303 COPD and chronic hypoxaemic respiratory failure to reduce exacerbation frequency
1304 and improve symptom control.

1305 ✓ Home HFNT could be considered in selected patients with bronchiectasis and ILD, but
1306 evidence is currently insufficient to recommend its routine use; where considered,
1307 treatment should form part of a specialist-led, individualised clinical management plan.

1308 ✓ The practical utility of HFNT is limited by the requirement for a power supply and circuit
1309 length.

1310 ✓ Early involvement of palliative teams should be considered when starting home HFNT
1311 in patients with advanced, progressive or life-limiting respiratory disease.

1312 ✓ An action plan for device management including servicing, failure, cleaning, and
1313 backup during disruption to power supply should be instituted prior to initiating home
1314 HFNT.

1315

1316 **Chronic hypercapnic respiratory failure**

1317 There is currently insufficient evidence that home HFNT is superior to NIV in COPD patients
1318 experiencing chronic hypercapnic respiratory failure (CHRF). Physiological data indicate
1319 non-inferiority compared to non-invasive ventilation with respect to PaCO₂ reduction and
1320 clinical trial data indicate an effect on time to first exacerbation in mild hypercapnia (PaCO₂
1321 <7 kPa). Home HFNT has not been evaluated in patients with non-COPD CHRF, therefore
1322 no recommendations can be made in this population.

1323

1324 **Chronic obstructive pulmonary disease**

1325 NIV is established as the standard of care to offload the respiratory muscle pump and improve
1326 physiological, clinical and patient-reported outcomes in patients with COPD and stable
1327 hypercapnia, as well as in those with persistent hypercapnia following AHRF. NIV is also
1328 widely used in other causes of CHRF, including obesity-related respiratory failure and
1329 neuromuscular disease.^{131–136}

1330 To date, domiciliary HFNT has been evaluated primarily in COPD populations with CHRF.
1331 Evidence remains limited, and prospective long-term data are required to clarify its role in both
1332 COPD and non-COPD populations.

1333 Direct physiological comparisons demonstrate reductions in CO₂ with both HFNT and NIV in
1334 stable hypercapnic COPD. Short-term crossover data suggest a greater CO₂ reduction with

NIV, while longer-term crossover studies have reported HFNT to be non-inferior within prespecified margins for CO₂ reduction. Interpretation is limited by small samples, heterogeneous treatment durations and differences in treatment adherence.^{137–139}

In a randomised crossover study conducted by Bräunlich et al., HFNT was reported to be non-inferior to NIV in terms of PaCO₂ reduction over a 6-week period.¹³⁹ Interpretation is limited by differential adherence between treatments and relatively low HFNT flow rates, including relatively low adherence to NIV (mean 3.9 hours/day), greater HFNT usage (5.2 hours/day), and the use of relatively low HFNT flow rates (20 L/min).

Nagata et al. have evaluated the clinical effects of domiciliary HFNT in combination with LTOT in stable hypercapnic COPD. In a randomised crossover trial, 6 weeks of HFNT plus LTOT was associated with improvements in dyspnoea and HRQoL, as well as reductions in both daytime and nocturnal PaCO₂, compared with LTOT alone.¹⁴⁰

In a subsequent 12-month randomised controlled trial, HFNT in combination with LTOT was associated with reduced exacerbation frequency and prolonged time to first exacerbation compared with LTOT alone.¹⁴¹ However, the study did not meet its target recruitment, and attrition introduced potential bias. No significant differences were observed in PaCO₂, exercise capacity or HRQoL at 12 months.

Meta-analysis of HFNT in hypercapnic COPD populations suggests a modest improvement in HRQoL, with a mean reduction in St George's Respiratory Questionnaire (SGRQ) score of 8.12 units (95% CI 2.95 to 13.30 lower), although the certainty of evidence is low and some included studies did not exclusively enrol hypercapnic patients.¹⁴²

In a pilot randomised crossover physiological study of 20 hypercapnic COPD patients recovering from acute exacerbation, asymmetric and standard HFNT interfaces produced similar overall PaCO₂ responses. In patients with more severe baseline hypercapnia, the asymmetric interface was associated with greater dead-space clearance and ventilatory efficiency.¹⁴³

Caution is warranted when applying HFNT in hypercapnic individuals. In the post-exacerbation setting following AHRF, differential effects have been observed, with one study reporting benefit in patients with COPD alone but not in those with coexistent COPD–obstructive sleep apnoea overlap syndrome. Trials of domiciliary HFNT have generally applied strict eligibility criteria and often excluded patients with higher BMI, recent acute NIV requirement, established domiciliary NIV, overlap syndrome or more severe ventilatory failure. This limits generalisability to patients with more severe disease or higher clinical instability.

Non-COPD populations

There is insufficient comparative evidence to support domiciliary HFNT in non-COPD causes of chronic hypercapnic respiratory failure.

Summary

- HFNT reduced PaCO₂ to a lesser extent than NIV in COPD patients with stable hypercapnia.

- 1376 ➤ HFNT with LTOT compared with LTOT alone reduced exacerbation rates, along with
1377 improving breathlessness and HRQoL scores in COPD patients with stable
1378 hypercapnia.
- 1379 ➤ Home HFNT may require monitoring to assess treatment response; optimal flow rates
1380 and treatment duration for CO₂ clearance are not established.
- 1381 ➤ Regulatory status and device indications for domiciliary HFNT vary by device and
1382 setting; clinicians should confirm local governance, commissioning and manufacturer
1383 guidance before initiation.
- 1384 ➤ There are no UK studies with health economic evaluation for the role of domiciliary
1385 HFNT.
- 1386 ➤ There is insufficient evidence to assess the use of domiciliary HFNT in management
1387 of CHRF in any patient group other than COPD.
- 1388

1389 ***Clinical practice points:***

- 1390 ✓ NIV remains the standard of care for patients with CHRF.
- 1391 ✓ Home HFNT may be considered in selected patients with stable COPD and CHRF
1392 where NIV is not tolerated or accepted; however, evidence specifically evaluating
1393 HFNT following NIV intolerance or failure is very limited, and NIV remains the
1394 established standard of care.
- 1395 ✓ Monitoring should be tailored to identify treatment failure, with individualised failure
1396 criteria and escalation plans based on the patient's clinical context and suitability for
1397 further respiratory support.
- 1398 ✓ There is insufficient evidence to advocate for home HFNT in stable COPD patients
1399 with PaCO₂ >7.0 kPa, persistent hypercapnia following an exacerbation with AHRF,
1400 COPD–OSA overlap, obesity-related respiratory failure, neuromuscular disease or
1401 other non-COPD causes of chronic hypercapnic respiratory failure.

Section 8: Practical aspects of managing HFNT in community settings

Clinical oversight of care

Evidence for community HFNT delivery remains limited. Home HFNT may be used as planned long-term therapy in selected patients with chronic respiratory disease or, in some circumstances, to facilitate discharge of patients who remain dependent on HFNT.¹²¹

Teams involved in the provision of HFNT at home may include acute and community respiratory teams, interstitial lung disease specialty multiprofessional teams, palliative care teams, complex home mechanical ventilation services, sleep and ventilation services, and home oxygen teams. It is important that such teams retain clinical oversight of the patient's overall condition during the transition from acute hospital to home. It is equally important to assure safe continuity of care in the community, and it should be recognised that the acute clinical team may lack the infrastructure to provide safe long-term care in the community. Care plans should define markers of deterioration, who should be contacted, and the appropriate escalation pathway, recognising the delays that can occur in the community when responding to acute clinical decline.^{122,144} In patients receiving HFNT with palliative intent or a treatment ceiling, anticipatory symptom-management plans should also be documented (see Section 10).

Familiarity with community HFNT devices and the ability to troubleshoot commonly encountered problems are vital. HFNT should be delivered through a service model with appropriate respiratory, oxygen, ventilation, community and palliative care expertise, with clear responsibility for both clinical oversight and equipment support. A regional shared-care model, similar to home ventilation services, may support safe implementation where local services do not have all required expertise.

Referral criteria

Referral criteria for home HFNT should be locally agreed upon and adapted as the evidence base evolves. Referring teams must understand the capabilities of community settings, particularly the trade-off between prescribed flow rate and FiO_2 .

For example, with two or three oxygen concentrators, the overall oxygen flow rate is unlikely to exceed 15 L/min. At 40 L/min of total flow, this would result in a delivered FiO_2 of just over 0.5. Increasing the total flow to 60 L/min would result in an FiO_2 of just over 0.4.

Some examples are given in the table below.

Oxygen flow rate ↓ Flow setting on HFNT machine →

	30	40	50	60
5	0.34	0.31	0.29	0.28
10	0.47	0.41	0.37	0.34
15	0.61	0.51	0.45	0.41

Table 4: Approximate delivered FiO_2 with different oxygen flow rates and total HFNT flow settings. Values are expressed as FiO_2 fractions. Values are illustrative estimates assuming supplemental oxygen at FiO_2 1.0 is blended with room air at FiO_2 0.21 to achieve the stated total flow. Actual inspired FiO_2 may be lower if patient inspiratory demand exceeds total HFNT flow because of additional room-air entrainment.¹¹

Transfer to the home/community setting

The transfer to home from an acute hospital is high-risk, particularly if the patient is unable to manage short periods of time off HFNT. Interruption of HFNT has caused serious harm during intrahospital transfer.¹⁴⁵ Accordingly, any transfer of an HFNT-dependent patient should include an explicit plan for continuity of respiratory support, compatible power and oxygen supplies, and an alternative strategy if HFNT cannot be maintained.

The receiving community team should have a documented handover and arrangements should be made to ensure that HFNT equipment is safely established and functioning at the destination.

Practical considerations in the community setting

Many devices used to deliver HFNT do not have an internal battery, while battery capability varies by device and should be confirmed before discharge or transfer. An individualised safety plan is therefore required. Patients dependent on electrically powered HFNT should be advised to register with their energy supplier's Priority Services Register and should have an individualised contingency plan for power interruption.¹⁴⁶

Home HFNT devices require regular device-specific cleaning and maintenance, which may necessitate interruption of therapy. Cleaning frequency and procedure should follow the manufacturer's instructions for the prescribed device. A clear, bespoke plan is therefore required to ensure patient safety during this period, which may require a second HFNT device or another mode of respiratory support, depending on the patient's clinical status and preferences. A lower-intensity oxygen device should not be assumed to provide equivalent support in an HFNT-dependent patient.¹⁴⁵

Patients receiving HFNT require a clear plan for what to do in the event of equipment failure. Where available, existing national guidance should be followed in terms of out-of-hours equipment replacement.¹⁴⁷

Commissioning

The commissioning arrangements will depend on the team delivering the clinical oversight of HFNT and their funding model (e.g., block contract, payment by results). Commissioning arrangements should reflect the complexity of the service and explicitly fund clinical oversight, equipment provision and maintenance, consumables, review and urgent troubleshooting. This ensures adequate funding for outpatient appointments and/or home visits. UK-specific health-economic evidence for domiciliary HFNT remains lacking.¹²¹

Local commissioning and service agreements should clearly define responsibility for provision and replacement of consumables.

Summary

- Evidence for domiciliary HFNT remains limited; current use includes planned long-term therapy in selected patients and, in some circumstances, facilitation of discharge for patients who remain HFNT-dependent.
- Delivery in the community requires coordinated multidisciplinary input, with clear clinical oversight to ensure continuity of care across acute and community teams.
- Shared-care models, like home ventilation services, may support safe and effective implementation.
- Referral criteria are not standardised and should reflect local capabilities, particularly limitations in oxygen delivery systems and the relationship between oxygen flow, total flow and achievable FiO₂.
- Transfer from hospital to home is a high-risk period, especially in patients unable to tolerate interruption of HFNT, and requires experienced teams and structured handover processes.
- Practical challenges include device power and battery limitations, potential interruption of therapy for device-specific cleaning and maintenance, and risks related to equipment failure or power loss, requiring individualised safety and contingency planning.
- Commissioning models vary, and there is currently no UK-specific health economic evidence to support widespread implementation, particularly in patients with complex or advanced respiratory disease.

Clinical practice points:

- ✓ Home HFNT delivery should involve liaison between acute and community multidisciplinary teams to support safe setup, clinical oversight and continuity of care.
- ✓ Transport of patients dependent on HFNT should be undertaken by appropriately trained transport or ambulance teams, with detailed handover to the receiving community team.
- ✓ Care plans should be developed for device management, transport and contingencies during device or power failure.

1510 ✓ Commissioning arrangements should be proportional to the complexity of the
1511 management of the home HFNT service and dependent on the local funding model.

1512

1513

1514

Consultation draft

Section 9: Secretion management

The use of HFNT to improve secretion burden and clearance in patients with chronic respiratory disease

Evidence for HFNT specifically as a secretion-management intervention remains limited and is derived mainly from small physiological studies and observational or exploratory clinical studies in bronchiectasis and COPD.^{7,125,126} Available data suggest HFNT may improve subjective mucus clearance and sputum expectoration in selected patients, but robust evidence for patient-important clinical outcomes remains limited.^{109,126}

Across available studies, HFNT has been associated with reductions in exacerbation frequency and hospitalisations in some chronic airway disease populations, although causality remains uncertain due to study design limitations.^{125–127,148} Further multicentre randomised controlled trials are required to define whether HFNT has a role as an adjunct to standard airway clearance strategies in COPD and bronchiectasis, including cystic fibrosis-related bronchiectasis.

Acute and short-term effects in airway disease

In a 15-patient feasibility study of acute exacerbations of COPD with bronchiectasis, Crimi et al. reported increased mucus production and improved self-reported ease of expectoration over 72 hours during HFNT at 50 L/min, with maximal effect observed after 24 hours of therapy.⁸⁵ HFNT was delivered at 37°C with FiO₂ titrated to maintain oxygen saturations ≥92%. Interpretation is limited by the single-arm design, small sample size and absence of comparison with standard pharmacological or physiotherapy-based airway clearance techniques.

Chronic respiratory disease and domiciliary HFNT

Bronchiectasis (non-cystic fibrosis)

In non-cystic fibrosis bronchiectasis, mucus burden and impaired clearance correlate with exacerbation frequency and quality of life impairment.

In a mixed COPD/bronchiectasis RCT, Rea et al. found fewer exacerbation days and a longer time to first exacerbation with long-term humidification therapy; annual exacerbation frequency was numerically lower (2.97 vs 3.63 per patient-year, $p=0.067$).¹²⁵ A subsequent bronchiectasis-specific post-hoc analysis of this cohort demonstrated a significant 31.3% reduction in exacerbation rate and improved HRQoL with HFNT.¹⁴⁸

Simioli et al. reported a reduction in exacerbation rate from 1.65 to 0.65 per year using HFNT at 35–60 L/min over a two-year crossover study, with reported adherence of ≥2 hours/day on at least 4 days per week.¹²⁷

Calabrese et al. reported significant reductions in annual exacerbation rate after 12 months of HFNT in both mild/moderate and severe bronchiectasis cohorts.¹⁴⁹

More recently, Crimi et al. demonstrated a significant reduction in CT mucus-plug burden following long-term HFNT in patients with bronchiectasis.¹⁵⁰

COPD

Although long-term HFNT trials in COPD have reported reductions in exacerbations and symptom burden, secretion-specific outcomes have rarely been primary endpoints.^{109,125} Direct evidence that HFNT improves mucus clearance in COPD therefore remains limited. The physiological effects of humidification and improved mucociliary function suggest a plausible mechanism for improved secretion clearance, but direct evidence in COPD populations remains limited.

In a 2025 mixed-methods feasibility RCT of home HFNT following severe AECOPD, D'Cruz et al. reported that quantitative cough scores did not clearly differ between groups, but participants using HFNT frequently reported looser sputum and easier secretion clearance.¹⁰⁹

Further studies are required to evaluate the effect of HFNT on secretion burden specifically in COPD populations.

Practical approaches to HFNT for secretion clearance

Home HFNT has demonstrated clinical benefit even with relatively short daily usage (approximately 1.7 hours/day).¹⁴⁸ Reported HFNT protocols vary considerably, with temperatures commonly around 37°C and flow rates ranging from approximately 20 to 60 L/min across studies.^{127,148} The optimal flow, temperature and daily duration for secretion management remain unknown.

Effective mucus clearance depends on airway-surface hydration, ciliary function, airway patency and sufficient expiratory airflow.^{151,152} These are impaired in obstructive lung disease due to reduced airway calibre and impaired ciliary function.

Physiotherapy and airway clearance

Airway clearance techniques (ACTs) are a core component of bronchiectasis management and should be individualised by appropriately trained respiratory physiotherapists. Where airway clearance is clinically indicated, HFNT should be regarded as a potential adjunct rather than a replacement for established ACTs.^{153–156}

Summary

- Evidence for HFNT in secretion management is limited and mainly derived from non-randomised, retrospective, and small prospective studies in COPD and bronchiectasis populations; hence HFNT should not replace physiotherapy-led airway clearance.
- HFNT may improve subjective mucus clearance and sputum expectoration in selected patients with acute exacerbations or stable chronic airway disease.
- In bronchiectasis, domiciliary HFNT has been associated with reduced exacerbation frequency, improved symptom burden, and improved quality of life in observational and crossover studies.
- In COPD, evidence for direct effects on sputum burden is limited, although improvements in symptoms and exacerbation-related outcomes have been reported in mixed populations and post-exacerbation recovery studies.

- 1596 ➤ Physiological plausibility is supported by heated humidification, improved airway-
1597 surface hydration and mucociliary function.
- 1598 ➤ Acute studies suggest HFNT may increase sputum production during exacerbations,
1599 but these findings are limited by small sample sizes and lack of control groups.
- 1600 ➤ Optimal HFNT settings and minimum effective daily duration for secretion
1601 management remain uncertain.
- 1602 ➤ All studies are limited by heterogeneity, small sample sizes, and risk of bias, with no
1603 robust randomised controlled trials specifically powered for secretion outcomes.
- 1604 ➤ HFNT should be considered an adjunct to, rather than a replacement for,
1605 physiotherapy-led airway clearance techniques.
- 1606 ➤ Evidence is insufficient to support HFNT as a primary stand-alone therapy for mucus
1607 clearance in either acute or domiciliary settings.

1608

1609 ***Clinical practice points:***

- 1610 ✓ There is a paucity of high-quality clinical trials evaluating HFNT for secretion
1611 management in both acute and chronic respiratory disease.
- 1612 ✓ HFNT should not be initiated primarily or solely for mucus clearance in acute
1613 respiratory failure.
- 1614 ✓ HFNT should not be initiated primarily or solely for mucus clearance in the domiciliary
1615 setting outside specialist respiratory supervision.
- 1616 ✓ Established physiotherapy-led ACTs should remain the primary airway-clearance
1617 strategy, while HFNT should be considered an adjunct rather than a replacement.

1618

Section 10: Withdrawal and palliation

Introduction

Withdrawal of respiratory support, including HFNT, may be required when treatment is no longer clinically effective, is no longer tolerated, or is inconsistent with patient preferences and goals of care. This may occur in the acute hospital setting or following anticipatory discussions in outpatient or community contexts.

Withdrawal may be considered where HFNT no longer provides overall clinical benefit, where its burdens outweigh its benefits, or where a patient with capacity chooses to discontinue treatment. Evidence specifically addressing HFNT withdrawal remains limited and is largely restricted to case-series data and expert guidance.¹⁵⁷ Practice is also informed by established experience with withdrawal of other forms of non-invasive respiratory support.^{158,159}

All withdrawal decisions should be considered within a palliative and end-of-life care framework, with early involvement of specialist palliative care teams.

Clinical context and withdrawal settings

Withdrawal of HFNT may occur in either acute or planned settings. Acute withdrawal typically occurs in hospital or hospice environments in patients with a prognosis of hours to days. These patients usually have advanced or irreversible respiratory failure, such as severe pneumonia or end-stage interstitial lung disease, where HFNT is providing essential oxygenation and respiratory support. In this context, withdrawal is often followed by rapid physiological deterioration and carries a high risk of distressing dyspnoea.¹⁵⁷

Planned withdrawal occurs in more stable patients whose decision is driven primarily by quality-of-life considerations rather than immediate physiological failure. These patients may still be partially dependent on HFNT, with support used predominantly for symptom relief rather than life-prolongation, although it can be a mixed picture. The trajectory following withdrawal is more variable and may range from hours to days, allowing for anticipatory planning and coordination of care in home, hospice, or inpatient settings.

It is important to distinguish between withdrawal of HFNT that will lead to death, and cessation of HFNT when it has been used as part of disease management but is no longer tolerated or indicated. For example, ceasing the use of 6 hours/day HFNT in hypoxaemic COPD to reduce exacerbations will not cause a deterioration towards death in the immediate hours or days and therefore is not classed as a withdrawal.

Acute withdrawal (hospital or hospice setting)

- Patients with prognosis of hours to days.
- Typically, severe or irreversible respiratory failure despite HFNT (e.g. pneumonia, advanced ILD).
- HFNT dependence is primarily related to oxygenation and respiratory-support requirements.
- Withdrawal usually results in rapid physiological deterioration.

- 1659 • High risk of severe dyspnoea and distress.
- 1660 • Requires frequent symptom assessment and anticipatory symptom control.

1661

1662 **Planned / domiciliary withdrawal (community or inpatient elective setting)**

- 1663 • Patients with more stable trajectories (days to weeks or longer prognosis).
- 1664 • Often driven by quality-of-life considerations rather than immediate physiological failure.
- 1665
- 1666 • HFNT dependence may be:
 - 1667 ○ partial oxygenation dependence, or
 - 1668 ○ predominantly symptom relief dependence (dyspnoea control rather than life-prolongation)
 - 1669
- 1670 • Time to deterioration is more variable (hours to days, sometimes longer).
- 1671 • Allows structured planning of location (home, hospice, hospital).
- 1672 • May be triggered by acute admission but still undertaken in a planned manner.

1673

1674 **Dependency phenotypes**

1675 For withdrawal planning, it may be clinically useful to distinguish patients who are
1676 predominantly dependent on HFNT for oxygenation from those in whom HFNT is being used
1677 predominantly for symptom relief. These categories are pragmatic rather than validated
1678 phenotypes and may overlap.

1679 In oxygenation-dependent patients, HFNT is primarily supporting gas exchange, and
1680 withdrawal typically results in rapid hypoxaemia and respiratory deterioration. These patients
1681 are considered highly dependent, with a high likelihood of rapid symptom escalation following
1682 withdrawal.

1683 In contrast, symptom-control-dependent patients use HFNT primarily for relief of dyspnoea,
1684 air hunger, or anxiety. In these patients, gas exchange may remain partially preserved without
1685 support, and the decline following withdrawal may be slower and more variable. These
1686 distinctions are clinically useful in anticipating symptom trajectory and guiding planning but
1687 should not replace individual assessment.

1688

1689 **Oxygenation-dependent patients**

- 1690 • HFNT primarily sustains gas exchange.
- 1691 • Withdrawal may lead to rapid worsening of gas exchange and respiratory distress.
- 1692 • High likelihood of rapid deterioration.
- 1693 • Requires intensive anticipatory prescribing and monitoring.

1694

Symptom-control–dependent patients

- HFNT is used primarily for relief of dyspnoea, air hunger, or anxiety.
- Gas exchange may be partially preserved off therapy.
- Deterioration may be slower and more variable.
- Greater emphasis on symptom-directed withdrawal strategies.

Medicolegal and ethical framework

Patients with fully informed capacity have a legal right to refuse or discontinue any medical treatment, including HFNT. Withdrawal of HFNT is legally considered withdrawal of treatment and is distinct from assisted dying or euthanasia.^{160–162} Where patients lack capacity, decisions must follow established legal frameworks. Valid and applicable advance decisions to refuse treatment must be respected. Where a lasting power of attorney for health and welfare is in place, decisions should be made in consultation with the appointed attorney. In the absence of these, a best interests decision must be made under the Mental Capacity Act 2005.¹⁶¹

Multidisciplinary decision-making is essential, with involvement of senior clinicians, typically respiratory or intensive care consultants. The underlying disease process remains the cause of death, rather than withdrawal of treatment.¹⁶⁰ Complex or disputed decisions should prompt senior multidisciplinary review and, where appropriate, independent clinical or ethics support. Unresolved significant disagreement may require legal advice and referral to the Court of Protection.¹⁶⁰

Such decisions, whilst grounded in a clear ethical and legal framework, can be emotive and challenging for the wider MDT. Clinical leadership should ensure that the rationale for decisions is clearly communicated and that staff are supported before, during and after withdrawal where needed.

Palliative care integration

Withdrawal of HFNT should be explicitly recognised as a palliative intervention. Early involvement of specialist palliative care teams is recommended to support symptom management, communication, and family support. Care should address physical symptoms such as dyspnoea, as well as psychological, emotional, and spiritual distress.

Some patients may continue to derive symptomatic benefit from HFNT until the end of life, and continuation of therapy may be appropriate where it aligns with patient goals and improves comfort.^{163,164}

The potential symptomatic benefits of HFNT should be balanced against treatment burden and its impact on place of care, as patients who become dependent on HFNT may be difficult to discharge where community HFNT is unavailable.¹⁶⁵

Withdrawal planning and escalation

Withdrawal of HFNT should be individualised and may be gradual or more rapid depending on clinical urgency and patient preference.¹⁵⁷ Some patients may prioritise awareness and

interaction during the dying phase, while others may prioritise symptom relief even at the expense of consciousness. The withdrawal strategy should therefore be tailored to patient values and documented preferences.¹⁶⁶

Pre-withdrawal planning

- Clear documentation of goals of care and agreed withdrawal plan.
- Identification of dependency phenotype (oxygenation vs symptom control).
- Anticipatory prescribing for:
 - dyspnoea (opioids)
 - anxiety/agitation (benzodiazepines)
- Agreement on preferred place of care (hospital, hospice, home).

Escalation plan during withdrawal

- Requires frequent reassessment of:
 - respiratory distress
 - anxiety/agitation
 - family distress
- Escalation of symptom control medications as required.
- Rapid access to senior clinician and palliative care support.
- Clear plan for conversion between oxygen delivery modalities if HFNT is discontinued abruptly or unintentionally.

Monitoring

- Focus is symptom-based rather than physiological targets.
- Monitoring includes:
 - respiratory distress scores (clinical observation)
 - comfort level and agitation
 - patient-reported breathlessness where possible
- Avoid burdensome or non-contributory physiological monitoring.

Practical symptom management considerations

Symptom control during withdrawal requires both pharmacological and non-pharmacological strategies. Breathlessness should be managed according to established palliative care principles, including the use of opioids and anxiolytics where appropriate. Guidance from

1769 chronic respiratory disease palliative frameworks, including those used in COPD and
1770 interstitial lung disease, supports structured symptom management approaches.^{166–168}

1771 Non-pharmacological measures for symptom management remain important. The use of
1772 handheld fans directed toward the face may reduce the sensation of breathlessness.¹⁶⁶
1773 Environmental modification, reassurance, and positioning strategies are also important
1774 components of care. Following withdrawal, regular mouth care and management of dry mouth
1775 should be provided according to patient need.¹⁶⁶ Replacement of HFNT flow with alternative
1776 oxygen delivery systems, such as nasal cannulae, Venturi masks, or reservoir masks, may be
1777 used depending on symptom burden and patient preference.

1778 See Appendix 4 for suggested flowchart for palliative withdrawal of HFNT.

1779

1780 **Summary**

- 1781 ➤ Evidence for HFNT withdrawal remains very limited, with no comparative trials of
1782 withdrawal strategies; available evidence comprises small case series, retrospective
1783 cohorts and expert guidance.
- 1784 ➤ Practice is extrapolated from withdrawal literature in NIV and acute respiratory support.
- 1785 ➤ Withdrawal may be considered where HFNT no longer provides overall clinical benefit,
1786 is not tolerated, or is inconsistent with patient preference, and may occur in acute or
1787 planned settings.
- 1788 ➤ Patients may be highly oxygenation-dependent or predominantly symptom-dependent,
1789 influencing symptom trajectory after withdrawal.
- 1790 ➤ The trajectory after withdrawal is variable and depends on underlying disease, degree
1791 of HFNT dependence and the extent to which HFNT is sustaining oxygenation versus
1792 providing symptom relief.
- 1793 ➤ Symptom burden, particularly dyspnoea and anxiety, is a key clinical challenge
1794 requiring anticipatory management.
- 1795 ➤ HFNT withdrawal is a palliative intervention requiring multidisciplinary, structured, and
1796 ethically grounded decision-making.

1797

1798 **Clinical practice points:**

- 1799 ✓ HFNT withdrawal should occur within a structured multidisciplinary and palliative care
1800 framework, with senior clinical leadership and early specialist palliative care
1801 involvement.
- 1802 ✓ Withdrawal planning should consider the distinction between oxygenation-dependent
1803 and symptom-control-dependent patients.
- 1804 ✓ Capacity assessment and legal frameworks (ADRT, LPA, MCA 2005) must be followed
1805 and documented.
- 1806 ✓ Withdrawal planning should include anticipatory prescribing for dyspnoea, anxiety, and
1807 terminal agitation.

- 1808 ✓ Non-pharmacological measures for symptom management, including fan therapy,
1809 mouth care and environmental optimisation, should be routinely used.
- 1810 ✓ Monitoring should prioritise comfort and symptom burden rather than physiological
1811 targets.
- 1812 ✓ Escalation pathways must be clearly defined, including access to senior clinicians and
1813 palliative care teams.
- 1814 ✓ Withdrawal may occur in hospital, hospice, or home settings depending on patient
1815 preference and clinical stability.
- 1816 ✓ Some patients may continue HFNT until death where symptom benefit outweighs
1817 burdens.
- 1818 ✓ Clear documentation of decision-making, rationale, and care plans is essential.
- 1819 ✓ Complex or disputed decisions should prompt senior multidisciplinary review and,
1820 where appropriate, independent clinical or ethics support; unresolved significant
1821 disagreement may require legal advice or referral to the Court of Protection.
- 1822
- 1823
- 1824

Section 11: Research recommendations and future priorities for HFNT

Introduction

HFNT is increasingly used across acute and chronic respiratory disease pathways, including ARF, chronic hypoxaemic respiratory failure, CHRF, secretion management in airway disease, and palliative respiratory care. Despite growing adoption, evidence gaps remain regarding optimal patient selection, treatment protocols, long-term clinical effectiveness, health economics, treatment burden, and integration into palliative and community respiratory pathways.

Current evidence is strongest in hypoxaemic ARF and COPD, while evidence in non-COPD populations, chronic domiciliary use, secretion management, and end-of-life withdrawal remains limited. Much of the existing literature comprises single-centre observational studies, physiological crossover studies, feasibility studies, or heterogeneous cohorts with variable treatment protocols.

This document outlines key research priorities and recommendations intended to guide future multicentre clinical trials, translational research, implementation science, and health service evaluation. Detailed research recommendations and future priorities across each clinical domain are provided in Appendix 5.

Overarching research priorities

Standardisation of HFNT Definitions and Protocols

Future studies should standardise:

- definitions of acute and chronic respiratory failure phenotypes
- flow rate protocols
- humidification temperature settings
- oxygen delivery strategies
- duration of therapy and adherence thresholds
- criteria for treatment escalation and failure
- definitions of respiratory-support dependence
- outcome reporting frameworks

Consensus definitions are required to improve comparability between studies and facilitate future meta-analysis.

Patient-centred outcomes

Future trials should prioritise:

- breathlessness scores
- HRQoL
- sleep quality
- symptom burden, patient comfort and treatment tolerance
- treatment burden, including equipment burden, noise, sleep disruption, mobility restriction and cleaning requirements
- functional status and physical activity
- carer burden
- place of care and place of death

1868 Many current studies focus predominantly on physiological endpoints while under-reporting
1869 patient-reported outcomes.

1870 **Long-term outcomes**

1871 Future research should evaluate different respiratory disease groups, reporting on:

- 1872 • long-term exacerbation frequency
- 1873 • hospitalisation rates
- 1874 • survival outcomes
- 1875 • longitudinal physiological trajectories
- 1876 • healthcare utilisation
- 1877 • cost-effectiveness
- 1878 • treatment adherence over time

1879 Longitudinal data extending beyond 12 months are currently sparse.

1880 **Health economic and sustainability evaluation**

1881 Robust health economic analyses are required across different respiratory disease groups,
1882 particularly in:

- 1883 • acute hospital use
- 1884 • hospital-at-home pathways
- 1885 • domiciliary HFNT provision
- 1886 • community respiratory care
- 1887 • palliative care settings

1888 Future evaluations should include:

- 1889 • QALYs
- 1890 • cost per admission avoided
- 1891 • community service utilisation
- 1892 • staffing implications
- 1893 • oxygen and equipment costs
- 1894 • informal caregiver burden
- 1895 • environmental impact and sustainability

1896

1897 **Conclusion**

1898 HFNT is increasingly integrated across acute, chronic, and palliative respiratory care
1899 pathways; however, major evidence gaps remain across virtually all indications outside
1900 hypoxaemic ARF.

1901 Future research priorities should focus on high-quality multicentre clinical trials, mechanistic
1902 physiology, implementation science, health economics, and patient-centred outcomes.
1903 Priorities include chronic domiciliary HFNT, secretion management, non-COPD respiratory
1904 failure, and palliative withdrawal pathways.

1905 Improved evidence will be essential to define evidence-based clinical practice guidance on
1906 the appropriate role of HFNT within modern respiratory medicine and ensure equitable,
1907 evidence-based, and patient-centred care.

1908

References

1. Nishimura M. High-Flow Nasal Cannula Oxygen Therapy in Adults: Physiological Benefits, Indication, Clinical Benefits, and Adverse Effects. *Respir Care* [Internet]. 2016 Apr;61(4):529–41. Available from: <http://dx.doi.org/10.4187/respcare.04577>
2. Natalini D, Grieco DL, Santantonio MT, Mincione L, Toni F, Anzellotti GM, et al. Physiological effects of high-flow oxygen in tracheostomized patients. *Ann Intensive Care* [Internet]. 2019 Oct 7;9(1):114. Available from: <http://dx.doi.org/10.1186/s13613-019-0591-y>
3. Alnajada A, Blackwood B, Messer B, Pavlov I, Shyamsundar M. International Survey of High-Flow Nasal Therapy Use for Respiratory Failure in Adult Patients. *J Clin Med* [Internet]. 2023 Jun 8;12(12). Available from: <http://dx.doi.org/10.3390/jcm12123911>
4. Crimi C, Noto A, Cortegiani A, Carlucci A, Gregoretti C, Inal-Ince D, et al. Practices of high-flow nasal therapy in acute and chronic respiratory failure: the Hi-Flow Survey. *BMJ Open Respir Res* [Internet]. 2025 Dec 18;12(1). Available from: <http://dx.doi.org/10.1136/bmjresp-2025-003547>
5. Spoletini G, Alotaibi M, Blasi F, Hill NS. Heated Humidified High-Flow Nasal Oxygen in Adults: Mechanisms of Action and Clinical Implications. *Chest* [Internet]. 2015 Jul;148(1):253–61. Available from: <http://dx.doi.org/10.1378/chest.14-2871>
6. Kilgour E, Rankin N, Ryan S, Pack R. Mucociliary function deteriorates in the clinical range of inspired air temperature and humidity. *Intensive Care Med* [Internet]. 2004 Jul;30(7):1491–4. Available from: <http://dx.doi.org/10.1007/s00134-004-2235-3>
7. Hasani A, Chapman TH, McCool D, Smith RE, Dilworth JP, Agnew JE. Domiciliary humidification improves lung mucociliary clearance in patients with bronchiectasis. *Chron Respir Dis* [Internet]. 2008;5(2):81–6. Available from: <http://dx.doi.org/10.1177/1479972307087190>
8. Möller W, Celik G, Feng S, Bartenstein P, Meyer G, Oliver E, et al. Nasal high flow clears anatomical dead space in upper airway models. *J Appl Physiol* (1985) [Internet]. 2015 Jun 15;118(12):1525–32. Available from: <http://dx.doi.org/10.1152/jappphysiol.00934.2014>
9. Tatkov S, Rees M, Gulley A, van den Heuvel LGT, Nilius G. Asymmetrical nasal high flow ventilation improves clearance of CO₂ from the anatomical dead space and increases positive airway pressure. *J Appl Physiol* (1985) [Internet]. 2023 Feb 1;134(2):365–77. Available from: <http://dx.doi.org/10.1152/jappphysiol.00692.2022>
10. Vieira F, Bezerra FS, Coudroy R, Schreiber A, Telias I, Dubo S, Cavalot G, Martins Pereira S, Piraino T, Brochard LJ. High-flow nasal cannula compared with continuous positive airway pressure: a bench and physiological study. *J Appl Physiol* (1985) [Internet]. 2022 Jun;132(6):1580–90. Available from: <http://dx.doi.org/10.1152/jappphysiol.00416.2021>
11. Ritchie JE, Williams AB, Gerard C, Hockey H. Evaluation of a humidified nasal high-flow oxygen system, using oxygraphy, capnography and measurement of upper airway pressures. *Anaesth Intensive Care* [Internet]. 2011 Nov;39(6):1103–10. Available from: <http://dx.doi.org/10.1177/0310057X1103900620>

- 1951 12. Parke RL, Eccleston ML, McGuinness SP. The effects of flow on airway pressure
1952 during nasal high-flow oxygen therapy. *Respir Care* [Internet]. 2011 Aug;56(8):1151–5.
1953 Available from: <http://dx.doi.org/10.4187/respcare.01106>
- 1954 13. Parke RL, Bloch A, McGuinness SP. Effect of Very-High-Flow Nasal Therapy on
1955 Airway Pressure and End-Expiratory Lung Impedance in Healthy Volunteers. *Respir*
1956 *Care* [Internet]. 2015 Oct;60(10):1397–403. Available from:
1957 <http://dx.doi.org/10.4187/respcare.04028>
- 1958 14. Mauri T, Turrini C, Eronia N, Grasselli G, Volta CA, Bellani G, et al. Physiologic
1959 Effects of High-Flow Nasal Cannula in Acute Hypoxemic Respiratory Failure. *Am J*
1960 *Respir Crit Care Med* [Internet]. 2017 May 1;195(9):1207–15. Available from:
1961 <http://dx.doi.org/10.1164/rccm.201605-0916OC>
- 1962 15. Pisani L, Fasano L, Corcione N, Comellini V, Musti MA, Brandao M, et al. Change
1963 in pulmonary mechanics and the effect on breathing pattern of high flow oxygen therapy
1964 in stable hypercapnic COPD. *Thorax* [Internet]. 2017 Apr;72(4):373–5. Available from:
1965 <http://dx.doi.org/10.1136/thoraxjnl-2016-209673>
- 1966 16. Di Mussi R, Spadaro S, Stripoli T, Volta CA, Trerotoli P, Pierucci P, et al. High-flow
1967 nasal cannula oxygen therapy decreases postextubation neuroventilatory drive and
1968 work of breathing in patients with chronic obstructive pulmonary disease. *Crit Care*
1969 [Internet]. 2018 Aug 2;22(1):180. Available from: [http://dx.doi.org/10.1186/s13054-018-](http://dx.doi.org/10.1186/s13054-018-2107-9)
1970 [2107-9](http://dx.doi.org/10.1186/s13054-018-2107-9)
- 1971 17. Williams R, Rankin N, Smith T, Galler D, Seakins P. Relationship between the
1972 humidity and temperature of inspired gas and the function of the airway mucosa. *Crit*
1973 *Care Med* [Internet]. 1996 Nov;24(11):1920–9. Available from:
1974 <http://dx.doi.org/10.1097/00003246-199611000-00025>
- 1975 18. Bräunlich J, Köhler M, Wirtz H. Nasal highflow improves ventilation in patients with
1976 COPD. *Int J Chron Obstruct Pulmon Dis* [Internet]. 2016 May 25;11:1077–85. Available
1977 from: <http://dx.doi.org/10.2147/COPD.S104616>
- 1978 19. Bräunlich J, Wirtz H. The impact of different prong-nares ratio on ventilation in
1979 COPD patients using nasal high-flow (NHF) - a physiological study. *BMC Pulm Med*
1980 [Internet]. 2024 Nov 18;24(1):573. Available from: [http://dx.doi.org/10.1186/s12890-024-](http://dx.doi.org/10.1186/s12890-024-03397-9)
1981 [03397-9](http://dx.doi.org/10.1186/s12890-024-03397-9)
- 1982 20. Heunks L, Schultz MJ. *ERS Practical Handbook of Invasive Mechanical Ventilation*
1983 [Internet]. European Respiratory Society; 2019. 308 p. Available from:
1984 https://play.google.com/store/books/details?id=E__YDwAAQBAJ
- 1985 21. O'Driscoll BR, Howard LS, Earis J, Mak V, British Thoracic Society Emergency
1986 Oxygen Guideline Group, BTS Emergency Oxygen Guideline Development Group. BTS
1987 guideline for oxygen use in adults in healthcare and emergency settings. *Thorax*
1988 [Internet]. 2017 Jun;72(Suppl 1):ii1–90. Available from:
1989 <http://dx.doi.org/10.1136/thoraxjnl-2016-209729>
- 1990 22. Oczkowski S, Ergon B, Bos L, Chatwin M, Ferrer M, Gregoretti C, et al. ERS clinical
1991 practice guidelines: high-flow nasal cannula in acute respiratory failure. *Eur Respir J*
1992 [Internet]. 2022 Apr;59(4). Available from: [http://dx.doi.org/10.1183/13993003.01574-](http://dx.doi.org/10.1183/13993003.01574-2021)
1993 [2021](http://dx.doi.org/10.1183/13993003.01574-2021)

- 1994 23. Frat JP, Quenot JP, Guitton C, Coudroy R, Gacouin A, Badie J, et al. High-Flow or
1995 Standard Oxygen in Acute Hypoxemic Respiratory Failure. *N Engl J Med* [Internet].
1996 2026 Mar 17; Available from: <http://dx.doi.org/10.1056/NEJMoa2516087>
- 1997 24. Lewis SR, Baker PE, Parker R, Smith AF. High-flow nasal cannulae for respiratory
1998 support in adult intensive care patients. *Cochrane Database Syst Rev* [Internet]. 2021
1999 Mar 4;3(3):CD010172. Available from:
2000 <http://dx.doi.org/10.1002/14651858.CD010172.pub3>
- 2001 25. Frat JP, Thille AW, Mercat A, Girault C, Ragot S, Perbet S, et al. High-flow oxygen
2002 through nasal cannula in acute hypoxemic respiratory failure. *N Engl J Med* [Internet].
2003 2015 Jun 4;372(23):2185–96. Available from:
2004 <http://dx.doi.org/10.1056/NEJMoa1503326>
- 2005 26. Jones PG, Kamona S, Doran O, Sawtell F, Wilsher M. Randomized Controlled Trial
2006 of Humidified High-Flow Nasal Oxygen for Acute Respiratory Distress in the Emergency
2007 Department: The HOT-ER Study. *Respir Care* [Internet]. 2016 Mar;61(3):291–9.
2008 Available from: <http://dx.doi.org/10.4187/respcare.04252>
- 2009 27. Makdee O, Monsomboon A, Surabenjawong U, Praphruekit N, Chaisirin W,
2010 Chakorn T, et al. High-Flow Nasal Cannula Versus Conventional Oxygen Therapy in
2011 Emergency Department Patients With Cardiogenic Pulmonary Edema: A Randomized
2012 Controlled Trial. *Ann Emerg Med* [Internet]. 2017 Oct;70(4):465–72.e2. Available from:
2013 <http://dx.doi.org/10.1016/j.annemergmed.2017.03.028>
- 2014 28. Azoulay E, Lemiale V, Mokart D, Nseir S, Argaud L, Pène F, et al. Effect of High-
2015 Flow Nasal Oxygen vs Standard Oxygen on 28-Day Mortality in Immunocompromised
2016 Patients With Acute Respiratory Failure: The HIGH Randomized Clinical Trial. *JAMA*
2017 [Internet]. 2018 Nov 27;320(20):2099–107. Available from:
2018 <http://dx.doi.org/10.1001/jama.2018.14282>
- 2019 29. Rochweg B, Granton D, Wang DX, Helviz Y, Einav S, Frat JP, et al. High flow
2020 nasal cannula compared with conventional oxygen therapy for acute hypoxemic
2021 respiratory failure: a systematic review and meta-analysis. *Intensive Care Med*
2022 [Internet]. 2019 May;45(5):563–72. Available from: [http://dx.doi.org/10.1007/s00134-](http://dx.doi.org/10.1007/s00134-019-05590-5)
2023 [019-05590-5](http://dx.doi.org/10.1007/s00134-019-05590-5)
- 2024 30. Ferreyro BL, Angriman F, Munshi L, Del Sorbo L, Ferguson ND, Rochweg B, et al.
2025 Association of Noninvasive Oxygenation Strategies With All-Cause Mortality in Adults
2026 With Acute Hypoxemic Respiratory Failure: A Systematic Review and Meta-analysis.
2027 *JAMA* [Internet]. 2020 Jul 7;324(1):57–67. Available from:
2028 <http://dx.doi.org/10.1001/jama.2020.9524>
- 2029 31. RENOVATE Investigators and the BRICNet Authors, Maia IS, Kawano-Dourado L,
2030 Tramuja L, de Oliveira NE, Souza RN, et al. High-Flow Nasal Oxygen vs Noninvasive
2031 Ventilation in Patients With Acute Respiratory Failure: The RENOVATE Randomized
2032 Clinical Trial. *JAMA* [Internet]. 2025 Mar 11;333(10):875–90. Available from:
2033 <http://dx.doi.org/10.1001/jama.2024.26244>
- 2034 32. Bell N, Hutchinson CL, Green TC, Rogan E, Bein KJ, Dinh MM. Randomised
2035 control trial of humidified high flow nasal cannulae versus standard oxygen in the

2036 emergency department. *Emerg Med Australas* [Internet]. 2015 Dec;27(6):537–41.
 2037 Available from: <http://dx.doi.org/10.1111/1742-6723.12490>

2038 33. Rittayamai N, Tscheikuna J, Praphruetkit N, Kijpinyochai S. Use of High-Flow Nasal
 2039 Cannula for Acute Dyspnea and Hypoxemia in the Emergency Department. *Respir Care*
 2040 [Internet]. 2015 Oct;60(10):1377–82. Available from:
 2041 <http://dx.doi.org/10.4187/respcare.03837>

2042 34. Azoulay E, Pickkers P, Soares M, Perner A, Rello J, Bauer PR, et al. Acute
 2043 hypoxemic respiratory failure in immunocompromised patients: the Efraim multinational
 2044 prospective cohort study. *Intensive Care Med* [Internet]. 2017 Dec;43(12):1808–19.
 2045 Available from: <http://dx.doi.org/10.1007/s00134-017-4947-1>

2046 35. Adda M, Coquet I, Darmon M, Thiery G, Schlemmer B, Azoulay E. Predictors of
 2047 noninvasive ventilation failure in patients with hematologic malignancy and acute
 2048 respiratory failure. *Crit Care Med* [Internet]. 2008 Oct;36(10):2766–72. Available from:
 2049 <http://dx.doi.org/10.1097/CCM.0b013e31818699f6>

2050 36. Molina R, Bernal T, Borges M, Zaragoza R, Bonastre J, Granada RM, et al.
 2051 Ventilatory support in critically ill hematology patients with respiratory failure. *Crit Care*
 2052 [Internet]. 2012 Jul 24;16(4):R133. Available from: <http://dx.doi.org/10.1186/cc11438>

2053 37. Azevedo LCP, Caruso P, Silva UVA, Torelly AP, Silva E, Rezende E, et al.
 2054 Outcomes for patients with cancer admitted to the ICU requiring ventilatory support:
 2055 results from a prospective multicenter study. *Chest* [Internet]. 2014 Aug;146(2):257–66.
 2056 Available from: <http://dx.doi.org/10.1378/chest.13-1870>

2057 38. Frat JP, Coudroy R, Marjanovic N, Thille AW. High-flow nasal oxygen therapy and
 2058 noninvasive ventilation in the management of acute hypoxemic respiratory failure. *Ann*
 2059 *Transl Med* [Internet]. 2017 Jul;5(14):297. Available from:
 2060 <http://dx.doi.org/10.21037/atm.2017.06.52>

2061 39. Lemiale V, Resche-Rigon M, Mokart D, Pène F, Argaud L, Mayaux J, et al. High-
 2062 Flow Nasal Cannula Oxygenation in Immunocompromised Patients With Acute
 2063 Hypoxemic Respiratory Failure: A Groupe de Recherche Respiratoire en Réanimation
 2064 Onco-Hématologique Study. *Crit Care Med* [Internet]. 2017 Mar;45(3):e274–80.
 2065 Available from: <http://dx.doi.org/10.1097/CCM.0000000000002085>

2066 40. Frat JP, Ragot S, Girault C, Perbet S, Prat G, Boulain T, et al. Effect of non-
 2067 invasive oxygenation strategies in immunocompromised patients with severe acute
 2068 respiratory failure: a post-hoc analysis of a randomised trial. *Lancet Respir Med*
 2069 [Internet]. 2016 Aug;4(8):646–52. Available from: [http://dx.doi.org/10.1016/S2213-2600\(16\)30093-5](http://dx.doi.org/10.1016/S2213-2600(16)30093-5)

2071 41. Roca O, de Acilu MG, Caralt B, Sacanell J, Masclans JR, ICU collaborators.
 2072 Humidified high flow nasal cannula supportive therapy improves outcomes in lung
 2073 transplant recipients readmitted to the intensive care unit because of acute respiratory
 2074 failure. *Transplantation* [Internet]. 2015 May;99(5):1092–8. Available from:
 2075 <http://dx.doi.org/10.1097/TP.0000000000000460>

2076 42. Cortegiani A, Crimi C, Sanfilippo F, Noto A, Di Falco D, Grasselli G, et al. High flow
 2077 nasal therapy in immunocompromised patients with acute respiratory failure: A

2078 systematic review and meta-analysis. *J Crit Care* [Internet]. 2019 Apr;50:250–6.
 2079 Available from: <http://dx.doi.org/10.1016/j.jcrc.2018.12.015>

2080 43. Cheng LC, Chang SP, Wang JJ, Hsiao SY, Lai CC, Chao CM. The Impact of High-
 2081 Flow Nasal Cannula on the Outcome of Immunocompromised Patients with Acute
 2082 Respiratory Failure: A Systematic Review and Meta-Analysis. *Medicina (Kaunas)*
 2083 [Internet]. 2019 Oct 16;55(10). Available from:
 2084 <http://dx.doi.org/10.3390/medicina55100693>

2085 44. Coudroy R, Jamet A, Petua P, Robert R, Frat JP, Thille AW. High-flow nasal
 2086 cannula oxygen therapy versus noninvasive ventilation in immunocompromised patients
 2087 with acute respiratory failure: an observational cohort study. *Ann Intensive Care*
 2088 [Internet]. 2016 Dec;6(1):45. Available from: [http://dx.doi.org/10.1186/s13613-016-0151-](http://dx.doi.org/10.1186/s13613-016-0151-7)
 2089 7

2090 45. Tu G, He H, Yin K, Ju M, Zheng Y, Zhu D, et al. High-flow Nasal Cannula Versus
 2091 Noninvasive Ventilation for Treatment of Acute Hypoxemic Respiratory Failure in Renal
 2092 Transplant Recipients. *Transplant Proc* [Internet]. 2017 Jul-Aug;49(6):1325–30.
 2093 Available from: <http://dx.doi.org/10.1016/j.transproceed.2017.03.088>

2094 46. Coudroy R, Frat JP, Ehrmann S, Pène F, Decavèle M, Terzi N, et al. High-flow
 2095 nasal oxygen alone or alternating with non-invasive ventilation in critically ill
 2096 immunocompromised patients with acute respiratory failure: a randomised controlled
 2097 trial. *Lancet Respir Med* [Internet]. 2022 Jul;10(7):641–9. Available from:
 2098 [http://dx.doi.org/10.1016/S2213-2600\(22\)00096-0](http://dx.doi.org/10.1016/S2213-2600(22)00096-0)

2099 47. Rello J, Storti E, Belliato M, Serrano R. Clinical phenotypes of SARS-CoV-2:
 2100 implications for clinicians and researchers. *Eur Respir J* [Internet]. 2020 May;55(5).
 2101 Available from: <http://dx.doi.org/10.1183/13993003.01028-2020>

2102 48. Ospina-Tascón GA, Calderón-Tapia LE, García AF, Zarama V, Gómez-Álvarez F,
 2103 Álvarez-Saa T, et al. Effect of High-Flow Oxygen Therapy vs Conventional Oxygen
 2104 Therapy on Invasive Mechanical Ventilation and Clinical Recovery in Patients With
 2105 Severe COVID-19: A Randomized Clinical Trial. *JAMA* [Internet]. 2021 Dec
 2106 7;326(21):2161–71. Available from: <http://dx.doi.org/10.1001/jama.2021.20714>

2107 49. Grieco DL, Menga LS, Cesarano M, Rosà T, Spadaro S, Bitondo MM, et al. Effect
 2108 of Helmet Noninvasive Ventilation vs High-Flow Nasal Oxygen on Days Free of
 2109 Respiratory Support in Patients With COVID-19 and Moderate to Severe Hypoxemic
 2110 Respiratory Failure: The HENIVOT Randomized Clinical Trial. *JAMA* [Internet]. 2021
 2111 May 4;325(17):1731–43. Available from: <http://dx.doi.org/10.1001/jama.2021.4682>

2112 50. Perkins GD, Ji C, Connolly BA, Couper K, Lall R, Baillie JK, et al. Effect of
 2113 Noninvasive Respiratory Strategies on Intubation or Mortality Among Patients With
 2114 Acute Hypoxemic Respiratory Failure and COVID-19: The RECOVERY-RS
 2115 Randomized Clinical Trial. *JAMA* [Internet]. 2022 Feb 8;327(6):546–58. Available from:
 2116 <http://dx.doi.org/10.1001/jama.2022.0028>

2117 51. Frat JP, Quenot JP, Badie J, Coudroy R, Guitton C, Ehrmann S, et al. Effect of
 2118 High-Flow Nasal Cannula Oxygen vs Standard Oxygen Therapy on Mortality in Patients
 2119 With Respiratory Failure Due to COVID-19: The SOHO-COVID Randomized Clinical

2120 Trial. JAMA [Internet]. 2022 Sep 27;328(12):1212–22. Available from:
 2121 <http://dx.doi.org/10.1001/jama.2022.15613>

2122 52. Bouadma L, Mekontso-Dessap A, Burdet C, Merdji H, Poissy J, Dupuis C, et al.
 2123 High-Dose Dexamethasone and Oxygen Support Strategies in Intensive Care Unit
 2124 Patients With Severe COVID-19 Acute Hypoxemic Respiratory Failure: The
 2125 COVIDICUS Randomized Clinical Trial. JAMA Intern Med [Internet]. 2022 Sep
 2126 1;182(9):906–16. Available from: <http://dx.doi.org/10.1001/jamainternmed.2022.2168>

2127 53. Crimi C, Noto A, Madotto F, Ippolito M, Nolasco S, Campisi R, et al. High-flow nasal
 2128 oxygen versus conventional oxygen therapy in patients with COVID-19 pneumonia and
 2129 mild hypoxaemia: a randomised controlled trial. Thorax [Internet]. 2023 Apr;78(4):354–
 2130 61. Available from: <http://dx.doi.org/10.1136/thoraxjnl-2022-218806>

2131 54. Pisciotto W, Passannante A, Arina P, Alotaibi K, Ambler G, Arulkumaran N. High-
 2132 flow nasal oxygen versus conventional oxygen therapy and noninvasive ventilation in
 2133 COVID-19 respiratory failure: a systematic review and network meta-analysis of
 2134 randomised controlled trials. Br J Anaesth [Internet]. 2024 May;132(5):936–44.
 2135 Available from: <http://dx.doi.org/10.1016/j.bja.2023.12.022>

2136 55. Li Y, Li C, Chang W, Liu L. High-flow nasal cannula reduces intubation rate in
 2137 patients with COVID-19 with acute respiratory failure: a meta-analysis and systematic
 2138 review. BMJ Open [Internet]. 2023 Mar 30;13(3):e067879. Available from:
 2139 <http://dx.doi.org/10.1136/bmjopen-2022-067879>

2140 56. Wang JC, Peng Y, Dai B, Hou HJ, Zhao HW, Wang W, et al. Comparison between
 2141 high-flow nasal cannula and conventional oxygen therapy in COVID-19 patients: a
 2142 systematic review and meta-analysis. Ther Adv Respir Dis [Internet]. 2024 Jan-
 2143 Dec;18:17534666231225323. Available from:
 2144 <http://dx.doi.org/10.1177/17534666231225323>

2145 57. Ryerson CJ, Collard HR. Update on the diagnosis and classification of ILD. Curr
 2146 Opin Pulm Med [Internet]. 2013 Sep;19(5):453–9. Available from:
 2147 <http://dx.doi.org/10.1097/MCP.0b013e328363f48d>

2148 58. Travis WD, Costabel U, Hansell DM, King TE Jr, Lynch DA, Nicholson AG, et al. An
 2149 official American Thoracic Society/European Respiratory Society statement: Update of
 2150 the international multidisciplinary classification of the idiopathic interstitial pneumonias.
 2151 Am J Respir Crit Care Med [Internet]. 2013 Sep 15;188(6):733–48. Available from:
 2152 <http://dx.doi.org/10.1164/rccm.201308-1483ST>

2153 59. Kondoh Y, Taniguchi H, Kawabata Y, Yokoi T, Suzuki K, Takagi K. Acute
 2154 exacerbation in idiopathic pulmonary fibrosis. Analysis of clinical and pathologic findings
 2155 in three cases. Chest [Internet]. 1993 Jun;103(6):1808–12. Available from:
 2156 <http://dx.doi.org/10.1378/chest.103.6.1808>

2157 60. Rangappa P, Moran JL. Outcomes of patients admitted to the intensive care unit
 2158 with idiopathic pulmonary fibrosis. Crit Care Resusc [Internet]. 2009 Jun;11(2):102–9.
 2159 Available from: <https://linkinghub.elsevier.com/retrieve/pii/S1441277223015338>

2160 61. Koyauchi T, Hasegawa H, Kanata K, Kakutani T, Amano Y, Ozawa Y, et al. Efficacy
 2161 and Tolerability of High-Flow Nasal Cannula Oxygen Therapy for Hypoxemic
 2162 Respiratory Failure in Patients with Interstitial Lung Disease with Do-Not-Intubate

2163 Orders: A Retrospective Single-Center Study. *Respiration* [Internet]. 2018 Jun
2164 28;96(4):323–9. Available from: <http://dx.doi.org/10.1159/000489890>

2165 62. Vianello A, Arcaro G, Molena B, Turato C, Braccioni F, Paladini L, et al. High-flow
2166 nasal cannula oxygen therapy to treat acute respiratory failure in patients with acute
2167 exacerbation of idiopathic pulmonary fibrosis. *Ther Adv Respir Dis* [Internet]. 2019 Jan-
2168 Dec;13:1753466619847130. Available from:
2169 <http://dx.doi.org/10.1177/1753466619847130>

2170 63. Pagliaro R, Aronne L, Fomez R, Ferri V, Montella A, Sanduzzi Zamparelli S, et al.
2171 High-Flow Nasal Cannula System in Respiratory Failure Associated with Interstitial Lung
2172 Diseases: A Systematic Review and Narrative Synthesis. *J Clin Med* [Internet]. 2024
2173 May 17;13(10). Available from: <http://dx.doi.org/10.3390/jcm13102956>

2174 64. McDonagh TA, Metra M, Adamo M, Gardner RS, Baumbach A, Böhm M, et al.
2175 2021 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure.
2176 *Eur Heart J* [Internet]. 2021 Sep 21;42(36):3599–726. Available from:
2177 <http://dx.doi.org/10.1093/eurheartj/ehab368>

2178 65. Masip J, Roque M, Sánchez B, Fernández R, Subirana M, Expósito JA.
2179 Noninvasive ventilation in acute cardiogenic pulmonary edema: systematic review and
2180 meta-analysis. *JAMA* [Internet]. 2005 Dec 28;294(24):3124–30. Available from:
2181 <http://dx.doi.org/10.1001/jama.294.24.3124>

2182 66. Roca O, Pérez-Terán P, Masclans JR, Pérez L, Galve E, Evangelista A, et al.
2183 Patients with New York Heart Association class III heart failure may benefit with high
2184 flow nasal cannula supportive therapy: high flow nasal cannula in heart failure. *J Crit*
2185 *Care* [Internet]. 2013 Oct;28(5):741–6. Available from:
2186 <http://dx.doi.org/10.1016/j.jcrc.2013.02.007>

2187 67. Yan L, Lu Y, Deng M, Zhang Q, Bian Y, Zhou X, et al. Efficacy of high-flow nasal
2188 cannula in patients with acute heart failure: a systematic review and meta-analysis.
2189 *BMC Pulm Med* [Internet]. 2023 Nov 28;23(1):476. Available from:
2190 <http://dx.doi.org/10.1186/s12890-023-02782-0>

2191 68. Fehrenbach H, Wagner C, Wegmann M. Airway remodeling in asthma: what really
2192 matters. *Cell Tissue Res* [Internet]. 2017 Mar;367(3):551–69. Available from:
2193 <http://dx.doi.org/10.1007/s00441-016-2566-8>

2194 69. Padem N, Saltoun C. Classification of asthma. *Allergy Asthma Proc* [Internet]. 2019
2195 Nov 1;40(6):385–8. Available from: <http://dx.doi.org/10.2500/aap.2019.40.4253>

2196 70. Papi A, Brightling C, Pedersen SE, Reddel HK. Asthma. *Lancet* [Internet]. 2018 Feb
2197 24;391(10122):783–800. Available from: [http://dx.doi.org/10.1016/S0140-](http://dx.doi.org/10.1016/S0140-6736(17)33311-1)
2198 [6736\(17\)33311-1](http://dx.doi.org/10.1016/S0140-6736(17)33311-1)

2199 71. Ramsahai JM, Hansbro PM, Wark PAB. Mechanisms and Management of Asthma
2200 Exacerbations. *Am J Respir Crit Care Med* [Internet]. 2019 Feb 15;199(4):423–32.
2201 Available from: <http://dx.doi.org/10.1164/rccm.201810-1931CI>

2202 72. Barnes PJ. Cellular and molecular mechanisms of asthma and COPD. *Clin Sci*
2203 (Lond) [Internet]. 2017 Jul 1;131(13):1541–58. Available from:
2204 <http://dx.doi.org/10.1042/CS20160487>

- 2205 73. Ruangsomboon O, Limsuwat C, Praphruekit N, Monsomboon A, Chakorn T. Nasal
2206 High-flow Oxygen Versus Conventional Oxygen Therapy for Acute Severe Asthma
2207 Patients: A Pilot Randomized Controlled Trial. *Acad Emerg Med* [Internet]. 2021
2208 May;28(5):530–41. Available from: <http://dx.doi.org/10.1111/acem.14187>
- 2209 74. Geng W, Batu W, You S, Tong Z, He H. High-Flow Nasal Cannula: A Promising
2210 Oxygen Therapy for Patients with Severe Bronchial Asthma Complicated with
2211 Respiratory Failure. *Can Respir J* [Internet]. 2020 Feb 20;2020:2301712. Available from:
2212 <http://dx.doi.org/10.1155/2020/2301712>
- 2213 75. Raeisi S, Fakharian A, Ghorbani F, Jamaati HR, Mirenayat MS. Value and Safety of
2214 High Flow Oxygenation in the Treatment of Inpatient Asthma: A Randomized, Double-
2215 blind, Pilot Study. *Iran J Allergy Asthma Immunol* [Internet]. 2019 Oct 16;18(6):615–23.
2216 Available from: <http://dx.doi.org/10.18502/ijaai.v18i6.2174>
- 2217 76. Ari A. Aerosol Drug Delivery Through High Flow Nasal Cannula. *Curr Pharm*
2218 *Biotechnol* [Internet]. 2017;18(11):877–82. Available from:
2219 <http://dx.doi.org/10.2174/1389201019666171219104217>
- 2220 77. Li J, Luo J, Chen Y, Xie L, Fink JB. Effects of flow rate on transnasal pulmonary
2221 aerosol delivery of bronchodilators via high-flow nasal cannula for patients with COPD
2222 and asthma: protocol for a randomised controlled trial. *BMJ Open* [Internet]. 2019 Jun
2223 24;9(6):e028584. Available from: <http://dx.doi.org/10.1136/bmjopen-2018-028584>
- 2224 78. Raskob GE, Angchaisuksiri P, Blanco AN, Büller H, Gallus A, Hunt BJ, et al.
2225 Thrombosis: a major contributor to global disease burden. *Semin Thromb Hemost*
2226 [Internet]. 2014 Oct;40(7):724–35. Available from: <http://dx.doi.org/10.1055/s-0034-1390325>
- 2227
- 2228 79. Burrowes KS, Clark AR, Tawhai MH. Blood flow redistribution and ventilation-
2229 perfusion mismatch during embolic pulmonary arterial occlusion. *Pulm Circ* [Internet].
2230 2011 Jul-Sep;1(3):365–76. Available from: <http://dx.doi.org/10.4103/2045-8932.87302>
- 2231 80. Messika J, Goutorbe P, Hajage D, Ricard JD. Severe pulmonary embolism
2232 managed with high-flow nasal cannula oxygen therapy. *Eur J Emerg Med* [Internet].
2233 2017 Jun;24(3):230–2. Available from:
2234 <http://dx.doi.org/10.1097/MEJ.0000000000000420>
- 2235 81. Aksakal A, Sağlam L, Kerget B, Yilmazel Uçar E. Comparison of the effectiveness
2236 of high-flow and conventional nasal cannula oxygen therapy in pulmonary embolism
2237 patients with acute hypoxemic respiratory failure. *Tuberk Toraks* [Internet]. 2021
2238 Dec;69(4):469–76. Available from: <http://dx.doi.org/10.5578/tt.20219604>
- 2239 82. Barker AF. Bronchiectasis. *N Engl J Med* [Internet]. 2002 May 2;346(18):1383–93.
2240 Available from: <http://dx.doi.org/10.1056/NEJMra012519>
- 2241 83. Goeminne PC, Nawrot TS, Rutters D, Seys S, Dupont LJ. Mortality in non-cystic
2242 fibrosis bronchiectasis: a prospective cohort analysis. *Respir Med* [Internet]. 2014
2243 Feb;108(2):287–96. Available from: <http://dx.doi.org/10.1016/j.rmed.2013.12.015>
- 2244 84. Goligher EC, Slutsky AS. Not Just Oxygen? Mechanisms of Benefit from High-Flow
2245 Nasal Cannula in Hypoxemic Respiratory Failure. *Am J Respir Crit Care Med* [Internet].

- 2246 2017 May 1;195(9):1128–31. Available from: [http://dx.doi.org/10.1164/rccm.201701-](http://dx.doi.org/10.1164/rccm.201701-0006ED)
2247 0006ED
- 2248 85. Crimi C, Noto A, Cortegiani A, Campisi R, Heffler E, Gregoretti C, et al. High Flow
2249 Nasal Therapy Use in Patients with Acute Exacerbation of COPD and Bronchiectasis: A
2250 Feasibility Study. *COPD* [Internet]. 2020 Apr;17(2):184–90. Available from:
2251 <http://dx.doi.org/10.1080/15412555.2020.1728736>
- 2252 86. Cuquemelle E, Pham T, Papon JF, Louis B, Danin PE, Brochard L. Heated and
2253 humidified high-flow oxygen therapy reduces discomfort during hypoxemic respiratory
2254 failure. *Respir Care* [Internet]. 2012 Oct;57(10):1571–7. Available from:
2255 <http://dx.doi.org/10.4187/respcare.01681>
- 2256 87. Sklar MC, Dres M, Rittayamai N, West B, Grieco DL, Telias I, et al. High-flow nasal
2257 oxygen versus noninvasive ventilation in adult patients with cystic fibrosis: a randomized
2258 crossover physiological study. *Ann Intensive Care* [Internet]. 2018 Sep 5;8(1):85.
2259 Available from: <http://dx.doi.org/10.1186/s13613-018-0432-4>
- 2260 88. Davidson AC, Banham S, Elliott M, Kennedy D, Gelder C, Glossop A, et al.
2261 BTS/ICS guideline for the ventilatory management of acute hypercapnic respiratory
2262 failure in adults. *Thorax* [Internet]. 2016 Apr;71 Suppl 2:ii1–35. Available from:
2263 <http://dx.doi.org/10.1136/thoraxjnl-2015-208209>
- 2264 89. Osadnik CR, Tee VS, Carson-Chahhoud KV, Picot J, Wedzicha JA, Smith BJ. Non-
2265 invasive ventilation for the management of acute hypercapnic respiratory failure due to
2266 exacerbation of chronic obstructive pulmonary disease. *Cochrane Database Syst Rev*
2267 [Internet]. 2017 Jul 13;7(7):CD004104. Available from:
2268 <http://dx.doi.org/10.1002/14651858.CD004104.pub4>
- 2269 90. Yang J, Chen L, Yu H, Hu J, Qiu F. Effects of high-flow nasal cannula oxygen
2270 therapy in bronchiectasis and hypercapnia: a retrospective observational study. *BMC*
2271 *Pulm Med* [Internet]. 2024 May 2;24(1):217. Available from:
2272 <http://dx.doi.org/10.1186/s12890-024-03037-2>
- 2273 91. Li XY, Tang X, Wang R, Yuan X, Zhao Y, Wang L, et al. High-Flow Nasal Cannula
2274 for Chronic Obstructive Pulmonary Disease with Acute Compensated Hypercapnic
2275 Respiratory Failure: A Randomized, Controlled Trial. *Int J Chron Obstruct Pulmon Dis*
2276 [Internet]. 2020 Nov 24;15:3051–61. Available from:
2277 <http://dx.doi.org/10.2147/COPD.S283020>
- 2278 92. Xia J, Gu S, Lei W, Zhang J, Wei H, Liu C, et al. High-flow nasal cannula versus
2279 conventional oxygen therapy in acute COPD exacerbation with mild hypercapnia: a
2280 multicenter randomized controlled trial. *Crit Care* [Internet]. 2022 Apr 15;26(1):109.
2281 Available from: <http://dx.doi.org/10.1186/s13054-022-03973-7>
- 2282 93. Pilcher J, Eastlake L, Richards M, Power S, Cripps T, Bibby S, et al. Physiological
2283 effects of titrated oxygen via nasal high-flow cannulae in COPD exacerbations: A
2284 randomized controlled cross-over trial. *Respirology* [Internet]. 2017 Aug;22(6):1149–55.
2285 Available from: <http://dx.doi.org/10.1111/resp.13050>
- 2286 94. Zhang L, Wang Y, Ye Y, Gao J, Zhu F, Min L. Comparison of High-Flow Nasal
2287 Cannula with Conventional Oxygen Therapy in Patients with Hypercapnic Chronic
2288 Obstructive Pulmonary Disease: A Systematic Review and Meta-Analysis. *Int J Chron*

- 2289 Obstruct Pulmon Dis [Internet]. 2023 May 16;18:895–906. Available from:
2290 <http://dx.doi.org/10.2147/COPD.S402506>
- 2291 95. Yuste ME, Moreno O, Narbona S, Acosta F, Peñas L, Colmenero M. Efficacy and
2292 safety of high-flow nasal cannula oxygen therapy in moderate acute hypercapnic
2293 respiratory failure. *Rev Bras Ter Intensiva* [Internet]. 2019 May 23;31(2):156–63.
2294 Available from: <http://dx.doi.org/10.5935/0103-507X.20190026>
- 2295 96. Lee MK, Choi J, Park B, Kim B, Lee SJ, Kim SH, et al. High flow nasal cannulae
2296 oxygen therapy in acute-moderate hypercapnic respiratory failure. *Clin Respir J*
2297 [Internet]. 2018 Jun;12(6):2046–56. Available from: <http://dx.doi.org/10.1111/crj.12772>
- 2298 97. Papachatzakis Y, Nikolaidis PT, Kontogiannis S, Trakada G. High-Flow Oxygen
2299 through Nasal Cannula vs. Non-Invasive Ventilation in Hypercapnic Respiratory Failure:
2300 A Randomized Clinical Trial. *Int J Environ Res Public Health* [Internet]. 2020 Aug
2301 18;17(16). Available from: <http://dx.doi.org/10.3390/ijerph17165994>
- 2302 98. Wang M, Zhao F, Sun L, Liang Y, Yan W, Sun X, et al. High-Flow Nasal Cannula
2303 versus Noninvasive Ventilation in AECOPD Patients with Respiratory Acidosis: A
2304 Retrospective Propensity Score-Matched Study. *Can Respir J* [Internet]. 2023 Apr
2305 15;2023:6377441. Available from: <http://dx.doi.org/10.1155/2023/6377441>
- 2306 99. Cong L, Zhou L, Liu H, Wang J. Outcomes of high-flow nasal cannula versus non-
2307 invasive positive pressure ventilation for patients with acute exacerbations of chronic
2308 obstructive pulmonary disease. *Int J Clin Exp Med*. 2019;12:10863–7.
- 2309 100. Doshi P, Whittle JS, Bublewicz M, Kearney J, Ashe T, Graham R, et al. High-
2310 Velocity Nasal Insufflation in the Treatment of Respiratory Failure: A Randomized
2311 Clinical Trial. *Ann Emerg Med* [Internet]. 2018 Jul;72(1):73–83.e5. Available from:
2312 <http://dx.doi.org/10.1016/j.annemergmed.2017.12.006>
- 2313 101. Ovtcharenko N, Ho E, Alhazzani W, Cortegiani A, Ergon B, Scala R, et al. High-
2314 flow nasal cannula versus non-invasive ventilation for acute hypercapnic respiratory
2315 failure in adults: a systematic review and meta-analysis of randomized trials. *Crit Care*
2316 [Internet]. 2022 Nov 9;26(1):348. Available from: <http://dx.doi.org/10.1186/s13054-022-04218-3>
- 2317
2318 102. Haciosman O, Ergenc H, Az A, Dogan Y, Sogut O. A high-flow nasal cannula
2319 versus noninvasive ventilation in acute exacerbations of chronic obstructive pulmonary
2320 disease. *Am J Emerg Med* [Internet]. 2025 Jan;87:38–43. Available from:
2321 <http://dx.doi.org/10.1016/j.ajem.2024.10.043>
- 2322 103. Cortegiani A, Longhini F, Madotto F, Groff P, Scala R, Crimi C, et al. High flow
2323 nasal therapy versus noninvasive ventilation as initial ventilatory strategy in COPD
2324 exacerbation: a multicenter non-inferiority randomized trial. *Crit Care* [Internet]. 2020
2325 Dec 14;24(1):692. Available from: <http://dx.doi.org/10.1186/s13054-020-03409-0>
- 2326 104. Pantazopoulos I, Boutlas S, Mavrovounis G, Papalampidou A, Papagiannakis N,
2327 Kontou M, et al. Nasal high flow or noninvasive ventilation? navigating hypercapnic
2328 COPD exacerbation treatment: A randomized noninferiority clinical trial. *Respir Med*
2329 [Internet]. 2024 Oct;232:107762. Available from:
2330 <http://dx.doi.org/10.1016/j.rmed.2024.107762>

- 2331 105. Tan D, Wang B, Cao P, Wang Y, Sun J, Geng P, et al. High flow nasal cannula
2332 oxygen therapy versus non-invasive ventilation for acute exacerbations of chronic
2333 obstructive pulmonary disease with acute-moderate hypercapnic respiratory failure: a
2334 randomized controlled non-inferiority trial. *Crit Care* [Internet]. 2024 Jul 18;28(1):250.
2335 Available from: <http://dx.doi.org/10.1186/s13054-024-05040-9>
- 2336 106. Zhong Z, Zhao L, Zhao Y, Li R, Xia S. Comparison of clinical outcomes between
2337 high-flow nasal cannula and non-invasive ventilation in acute exacerbation of COPD: a
2338 meta-analysis of randomized controlled trials. *BMC Pulm Med* [Internet]. 2025 Aug
2339 26;25(1):405. Available from: <http://dx.doi.org/10.1186/s12890-025-03873-w>
- 2340 107. Spoletini G, Mega C, Pisani L, Alotaibi M, Khoja A, Price LL, et al. High-flow nasal
2341 therapy vs standard oxygen during breaks off noninvasive ventilation for acute
2342 respiratory failure: A pilot randomized controlled trial. *J Crit Care* [Internet]. 2018
2343 Dec;48:418–25. Available from: <http://dx.doi.org/10.1016/j.jcrc.2018.10.004>
- 2344 108. Longhini F, Pisani L, Lungu R, Comellini V, Bruni A, Garofalo E, et al. High-Flow
2345 Oxygen Therapy After Noninvasive Ventilation Interruption in Patients Recovering From
2346 Hypercapnic Acute Respiratory Failure: A Physiological Crossover Trial. *Crit Care Med*
2347 [Internet]. 2019 Jun;47(6):e506–11. Available from:
2348 <http://dx.doi.org/10.1097/CCM.00000000000003740>
- 2349 109. D'Cruz RF, Rossel A, Kaltsakas G, Suh ES, Douiri A, Rose L, et al. Home high-
2350 flow therapy during recovery from severe chronic obstructive pulmonary disease
2351 (COPD) exacerbation: a mixed-methods feasibility randomised control trial. *BMJ Open*
2352 *Respir Res* [Internet]. 2025 Jan 6;12(1). Available from:
2353 <http://dx.doi.org/10.1136/bmjresp-2024-002698>
- 2354 110. Bouhassira DC, Hochberg CH, Sahetya SK, Parker A, Aziz KB, Yan L, et al.
2355 Patterns and outcomes of real-world high-flow nasal cannula use: a multi-hospital
2356 retrospective cohort study. *Crit Care Sci* [Internet]. 2026 Mar 13;38:e20260366.
2357 Available from: <http://dx.doi.org/10.62675/2965-2774.20260366>
- 2358 111. Royal College of Physicians. National Early Warning Score (NEWS) 2:
2359 Standardising the assessment of acute-illness severity in the NHS [Internet]. RCP; 2017
2360 [cited 2026 Aug 24]. Available from: [https://www.rcp.ac.uk/media/a4ibkbbf/news2-final-](https://www.rcp.ac.uk/media/a4ibkbbf/news2-final-report_0_0.pdf)
2361 [report_0_0.pdf](https://www.rcp.ac.uk/media/a4ibkbbf/news2-final-report_0_0.pdf)
- 2362 112. Respiratory Support National Audit 2023 [Internet]. [cited 2026 May 7]. Available
2363 from: [https://www.brit-thoracic.org.uk/clinical-resources/clinical-audits/respiratory-](https://www.brit-thoracic.org.uk/clinical-resources/clinical-audits/respiratory-support-national-audit-2023/)
2364 [support-national-audit-2023/](https://www.brit-thoracic.org.uk/clinical-resources/clinical-audits/respiratory-support-national-audit-2023/)
- 2365 113. Davies M, Allen M, Bentley A, Bourke SC, Creagh-Brown B, D'Oliveiro R, et al.
2366 British Thoracic Society Quality Standards for acute non-invasive ventilation in adults.
2367 *BMJ Open Respir Res* [Internet]. 2018 Apr 5;5(1):e000283. Available from:
2368 <http://dx.doi.org/10.1136/bmjresp-2018-000283>
- 2369 114. Messer B, Allen M, Antoine-Pitterson P, Blundell A, Davies M, Moonesinghe R, et
2370 al. Respiratory Support Units: Guidance on development and implementation [Internet].
2371 The British Thoracic Society and the Intensive Care Society ; 2021 Jun. (British
2372 Thoracic Society Reports; vol. 12). Available from: <https://www.brit->

2373 thoracic.org.uk/document-library/delivery-of-care/respiratory-support-units/respiratory-
2374 support-units-guidance-on-development-and-implementation/

2375 115. Roca O, Caralt B, Messika J, Samper M, Sztrymf B, Hernández G, et al. An Index
2376 Combining Respiratory Rate and Oxygenation to Predict Outcome of Nasal High-Flow
2377 Therapy. *Am J Respir Crit Care Med* [Internet]. 2019 Jun 1;199(11):1368–76. Available
2378 from: <http://dx.doi.org/10.1164/rccm.201803-0589OC>

2379 116. Kang BJ, Koh Y, Lim CM, Huh JW, Baek S, Han M, et al. Failure of high-flow
2380 nasal cannula therapy may delay intubation and increase mortality. *Intensive Care Med*
2381 [Internet]. 2015 Apr;41(4):623–32. Available from: <http://dx.doi.org/10.1007/s00134-015-3693-5>

2383 117. Storgaard LH, Hockey HU, Laursen BS, Weinreich UM. Long-term effects of
2384 oxygen-enriched high-flow nasal cannula treatment in COPD patients with chronic
2385 hypoxemic respiratory failure. *Int J Chron Obstruct Pulmon Dis* [Internet]. 2018 Apr
2386 16;13:1195–205. Available from: <http://dx.doi.org/10.2147/COPD.S159666>

2387 118. Cirio S, Piran M, Vitacca M, Piaggi G, Ceriana P, Prazzoli M, et al. Effects of
2388 heated and humidified high flow gases during high-intensity constant-load exercise on
2389 severe COPD patients with ventilatory limitation. *Respir Med* [Internet]. 2016
2390 Sep;118:128–32. Available from: <http://dx.doi.org/10.1016/j.rmed.2016.08.004>

2391 119. Chatila W, Nugent T, Vance G, Gaughan J, Criner GJ. The effects of high-flow vs
2392 low-flow oxygen on exercise in advanced obstructive airways disease. *Chest* [Internet].
2393 2004 Oct;126(4):1108–15. Available from: <http://dx.doi.org/10.1378/chest.126.4.1108>

2394 120. Prieur G, Delorme M, Lebreton M, Combret Y, Machefert M, Medrinal C, et al. Nasal
2395 High-Flow Therapy during Exercise in Patients with Chronic Obstructive Pulmonary
2396 Disease: A Systematic Review and Meta-Analysis. *Ann Am Thorac Soc* [Internet]. 2022
2397 Feb;19(2):291–302. Available from: <http://dx.doi.org/10.1513/AnnalsATS.202104-436SR>

2398 121. Jácome C, Jácome M, Correia S, Flores I, Farinha P, Duarte M, et al.
2399 Effectiveness, Adherence and Safety of Home High Flow Nasal Cannula in Chronic
2400 Respiratory Disease and Respiratory Insufficiency: A Systematic Review. *Arch*
2401 *Bronconeumol* [Internet]. 2024 Aug;60(8):490–502. Available from:
2402 <http://dx.doi.org/10.1016/j.arbres.2024.05.001>

2403 122. Hardinge M, Annandale J, Bourne S, Cooper B, Evans A, Freeman D, et al. British
2404 Thoracic Society guidelines for home oxygen use in adults. *Thorax* [Internet]. 2015
2405 Jun;70 Suppl 1:i1–43. Available from: <http://dx.doi.org/10.1136/thoraxjnl-2015-206865>

2406 123. Fraser JF, Spooner AJ, Dunster KR, Anstey CM, Corley A. Nasal high flow oxygen
2407 therapy in patients with COPD reduces respiratory rate and tissue carbon dioxide while
2408 increasing tidal and end-expiratory lung volumes: a randomised crossover trial. *Thorax*
2409 [Internet]. 2016 Aug;71(8):759–61. Available from: <http://dx.doi.org/10.1136/thoraxjnl-2015-207962>

2411 124. Sørensen SS, Storgaard LH, Weinreich UM. Cost-Effectiveness of Domiciliary
2412 High Flow Nasal Cannula Treatment in COPD Patients with Chronic Respiratory Failure.
2413 *Clinicoecon Outcomes Res* [Internet]. 2021 Jun 18;13:553–64. Available from:
2414 <http://dx.doi.org/10.2147/CEOR.S312523>

- 2415 125. Rea H, McAuley S, Jayaram L, Garrett J, Hockey H, Storey L, et al. The clinical
2416 utility of long-term humidification therapy in chronic airway disease. *Respir Med*
2417 [Internet]. 2010 Apr;104(4):525–33. Available from:
2418 <http://dx.doi.org/10.1016/j.rmed.2009.12.016>
- 2419 126. Crimi C, Nolasco S, Campisi R, Nigro M, Impellizzeri P, Cortegiani A, et al. Long-
2420 Term Domiciliary High-Flow Nasal Therapy in Patients with Bronchiectasis: A
2421 Preliminary Retrospective Observational Case-Control Study. *J Clin Med* [Internet].
2422 2022 Dec 9;11(24). Available from: <http://dx.doi.org/10.3390/jcm11247323>
- 2423 127. Simioli F, Fiorentino G, Cauteruccio R, Coppola A, Imitazione P, Marotta A, et al.
2424 Long-Term High Flow Nasal Cannula Therapy in Primary and Secondary
2425 Bronchiectasis. *Healthcare (Basel)* [Internet]. 2023 Apr 27;11(9). Available from:
2426 <http://dx.doi.org/10.3390/healthcare11091250>
- 2427 128. Weinreich UM, Burchardt C, Huremovic J. The effect of domiciliary high flow nasal
2428 cannula treatment on dyspnea and walking distance in patients with interstitial lung
2429 disease - A pilot study. *Chron Respir Dis* [Internet]. 2022 Jan-
2430 Dec;19:14799731221137085. Available from:
2431 <http://dx.doi.org/10.1177/14799731221137085>
- 2432 129. Harada J, Nagata K, Morimoto T, Iwata K, Matsunashi A, Sato Y, et al. Effect of
2433 high-flow nasal cannula oxygen therapy on exercise tolerance in patients with idiopathic
2434 pulmonary fibrosis: A randomized crossover trial. *Respirology* [Internet]. 2022
2435 Feb;27(2):144–51. Available from: <http://dx.doi.org/10.1111/resp.14176>
- 2436 130. Suzuki A, Ando M, Kimura T, Kataoka K, Yokoyama T, Shiroshita E, et al. The
2437 impact of high-flow nasal cannula oxygen therapy on exercise capacity in fibrotic
2438 interstitial lung disease: a proof-of-concept randomized controlled crossover trial. *BMC*
2439 *Pulm Med* [Internet]. 2020 Feb 24;20(1):51. Available from:
2440 <http://dx.doi.org/10.1186/s12890-020-1093-2>
- 2441 131. Köhnlein T, Windisch W, Köhler D, Drabik A, Geiseler J, Hartl S, et al. Non-
2442 invasive positive pressure ventilation for the treatment of severe stable chronic
2443 obstructive pulmonary disease: a prospective, multicentre, randomised, controlled
2444 clinical trial. *Lancet Respir Med* [Internet]. 2014 Sep;2(9):698–705. Available from:
2445 [http://dx.doi.org/10.1016/S2213-2600\(14\)70153-5](http://dx.doi.org/10.1016/S2213-2600(14)70153-5)
- 2446 132. Murphy PB, Rehal S, Arbane G, Bourke S, Calverley PMA, Crook AM, et al. Effect
2447 of Home Noninvasive Ventilation With Oxygen Therapy vs Oxygen Therapy Alone on
2448 Hospital Readmission or Death After an Acute COPD Exacerbation: A Randomized
2449 Clinical Trial. *JAMA* [Internet]. 2017 Jun 6;317(21):2177–86. Available from:
2450 <http://dx.doi.org/10.1001/jama.2017.4451>
- 2451 133. Struik FM, Sprooten RTM, Kerstjens HAM, Bladder G, Zijnen M, Asin J, et al.
2452 Nocturnal non-invasive ventilation in COPD patients with prolonged hypercapnia after
2453 ventilatory support for acute respiratory failure: a randomised, controlled, parallel-group
2454 study. *Thorax* [Internet]. 2014 Sep;69(9):826–34. Available from:
2455 <http://dx.doi.org/10.1136/thoraxjnl-2014-205126>
- 2456 134. Bourke SC, Tomlinson M, Williams TL, Bullock RE, Shaw PJ, Gibson GJ. Effects
2457 of non-invasive ventilation on survival and quality of life in patients with amyotrophic

2458 lateral sclerosis: a randomised controlled trial. *Lancet Neurol* [Internet]. 2006
 2459 Feb;5(2):140–7. Available from: [http://dx.doi.org/10.1016/S1474-4422\(05\)70326-4](http://dx.doi.org/10.1016/S1474-4422(05)70326-4)

2460 135. Mokhlesi B, Masa JF, Brozek JL, Gurubhagavatula I, Murphy PB, Piper AJ, et al.
 2461 Evaluation and Management of Obesity Hypoventilation Syndrome. An Official
 2462 American Thoracic Society Clinical Practice Guideline. *Am J Respir Crit Care Med*
 2463 [Internet]. 2019 Aug 1;200(3):e6–24. Available from:
 2464 <http://dx.doi.org/10.1164/rccm.201905-1071ST>

2465 136. Macrea M, Oczkowski S, Rochweg B, Branson RD, Celli B, Coleman JM 3rd, et
 2466 al. Long-Term Noninvasive Ventilation in Chronic Stable Hypercapnic Chronic
 2467 Obstructive Pulmonary Disease. An Official American Thoracic Society Clinical Practice
 2468 Guideline. *Am J Respir Crit Care Med* [Internet]. 2020 Aug 15;202(4):e74–87. Available
 2469 from: <http://dx.doi.org/10.1164/rccm.202006-2382ST>

2470 137. Bräunlich J, Seyfarth HJ, Wirtz H. Nasal High-flow versus non-invasive ventilation
 2471 in stable hypercapnic COPD: a preliminary report. *Multidiscip Respir Med* [Internet].
 2472 2015 Sep 3;10(1):27. Available from: <http://dx.doi.org/10.1186/s40248-015-0019-y>

2473 138. McKinstry S, Singer J, Baarsma JP, Weatherall M, Beasley R, Fingleton J. Nasal
 2474 high-flow therapy compared with non-invasive ventilation in COPD patients with chronic
 2475 respiratory failure: A randomized controlled cross-over trial. *Respirology* [Internet]. 2019
 2476 Nov;24(11):1081–7. Available from: <http://dx.doi.org/10.1111/resp.13575>

2477 139. Bräunlich J, Dellweg D, Bastian A, Budweiser S, Randerath W, Triché D, et al.
 2478 Nasal high-flow versus noninvasive ventilation in patients with chronic hypercapnic
 2479 COPD. *Int J Chron Obstruct Pulmon Dis* [Internet]. 2019 Jul 5;14:1411–21. Available
 2480 from: <http://dx.doi.org/10.2147/COPD.S206111>

2481 140. Nagata K, Kikuchi T, Horie T, Shiraki A, Kitajima T, Kadowaki T, et al. Domiciliary
 2482 High-Flow Nasal Cannula Oxygen Therapy for Patients with Stable Hypercapnic
 2483 Chronic Obstructive Pulmonary Disease. A Multicenter Randomized Crossover Trial.
 2484 *Ann Am Thorac Soc* [Internet]. 2018 Apr;15(4):432–9. Available from:
 2485 <http://dx.doi.org/10.1513/AnnalsATS.201706-425OC>

2486 141. Nagata K, Horie T, Chohnabayashi N, Jinta T, Tsugitomi R, Shiraki A, et al. Home
 2487 High-Flow Nasal Cannula Oxygen Therapy for Stable Hypercapnic COPD: A
 2488 Randomized Clinical Trial. *Am J Respir Crit Care Med* [Internet]. 2022 Dec
 2489 1;206(11):1326–35. Available from: <http://dx.doi.org/10.1164/rccm.202201-0199OC>

2490 142. Pitre T, Abbasi S, Su J, Mah J, Zeraatkar D. Home high flow nasal cannula for
 2491 chronic hypercapnic respiratory failure in COPD: A systematic review and meta-
 2492 analysis. *Respir Med* [Internet]. 2023 Oct 5;219:107420. Available from:
 2493 <http://dx.doi.org/10.1016/j.rmed.2023.107420>

2494 143. Pisani L, Vega ML, Ageno E, Prediletto I, Dongilli R, Catalanotti V, et al. Effects of
 2495 asymmetric nasal high-flow cannula on carbon dioxide in hypercapnic patients: A
 2496 randomised crossover physiological pilot study. *Pulmonology* [Internet]. 2025 Dec
 2497 31;31(1):2411813. Available from: <http://dx.doi.org/10.1080/25310429.2024.2411813>

2498 144. Suntharalingam J, Wilkinson T, Annandale J, Davey C, Fielding R, Freeman D, et
 2499 al. British Thoracic Society quality standards for home oxygen use in adults. *BMJ Open*

2500 Respir Res [Internet]. 2017 Sep 18;4(1):e000223. Available from:
2501 <http://dx.doi.org/10.1136/bmjresp-2017-000223>

2502 145. NHS England and NHS Improvement. Interruption of high flow nasal oxygen
2503 during transfer [Internet]. NHS England and NHS Improvement; 2020 Apr [cited 2026
2504 May 7]. (National Patient Safety Alert NatPSA/2020/002/NHSPS). Available from:
2505 [https://www.england.nhs.uk/2020/04/interruption-of-high-flow-nasal-oxygen-during-](https://www.england.nhs.uk/2020/04/interruption-of-high-flow-nasal-oxygen-during-transfer/)
2506 [transfer/](https://www.england.nhs.uk/2020/04/interruption-of-high-flow-nasal-oxygen-during-transfer/)

2507 146. Ofgem. Join your supplier's Priority Services Register [Internet]. Ofgem. [cited
2508 2026 Aug 24]. Available from: [https://www.ofgem.gov.uk/information-consumers/energy-](https://www.ofgem.gov.uk/information-consumers/energy-advice-households/join-your-suppliers-priority-services-register)
2509 [advice-households/join-your-suppliers-priority-services-register](https://www.ofgem.gov.uk/information-consumers/energy-advice-households/join-your-suppliers-priority-services-register)

2510 147. Messer B, Allen M, Armstrong A, Bentley A, Davies M, Felton T, et al. Model of
2511 Care for Complex Home Mechanical Ventilation [Internet]. The British Thoracic Society;
2512 2024 [cited 2026 Aug 24]. (British Thoracic Society Reports; vol. 15). Available from:
2513 [https://www.brit-thoracic.org.uk/document-library/delivery-of-care/model-of-care-for-](https://www.brit-thoracic.org.uk/document-library/delivery-of-care/model-of-care-for-complex-home-ventilation/bts-model-of-care-for-complex-home-mechanical-ventilation/)
2514 [complex-home-ventilation/bts-model-of-care-for-complex-home-mechanical-ventilation/](https://www.brit-thoracic.org.uk/document-library/delivery-of-care/model-of-care-for-complex-home-ventilation/bts-model-of-care-for-complex-home-mechanical-ventilation/)

2515 148. Good WR, Garrett J, Hockey HUP, Jayaram L, Wong C, Rea H. The role of high-
2516 flow nasal therapy in bronchiectasis: a post hoc analysis. ERJ Open Res [Internet].
2517 2021 Jan;7(1). Available from: <http://dx.doi.org/10.1183/23120541.00711-2020>

2518 149. Calabrese C, Nolasco S, Annunziata A, Sola A, Imitazione P, Campisi R, et al.
2519 Long-Term High-Flow Nasal Therapy in Patients with Bronchiectasis of Different
2520 Severity: A Retrospective Cohort Study. J Clin Med [Internet]. 2024 Oct 15;13(20).
2521 Available from: <http://dx.doi.org/10.3390/jcm13206146>

2522 150. Crimi C, Nolasco S, Campisi R, Nigro M, Impellizzeri P, Cortegiani A, et al. Impact
2523 of long-term high-flow nasal therapy on mucus plugs in patients with bronchiectasis.
2524 ERJ Open Res [Internet]. 2025 May;11(3). Available from:
2525 <http://dx.doi.org/10.1183/23120541.00962-2024>

2526 151. Button BM, Button B. Structure and function of the mucus clearance system of the
2527 lung. Cold Spring Harb Perspect Med [Internet]. 2013 Aug 1;3(8). Available from:
2528 <http://dx.doi.org/10.1101/cshperspect.a009720>

2529 152. Hill DB, Button B, Rubinstein M, Boucher RC. Physiology and pathophysiology of
2530 human airway mucus. Physiol Rev [Internet]. 2022 Oct 1;102(4):1757–836. Available
2531 from: <http://dx.doi.org/10.1152/physrev.00004.2021>

2532 153. Hill AT, Sullivan AL, Chalmers JD, De Soyza A, Elborn SJ, Floto AR, et al. British
2533 Thoracic Society Guideline for bronchiectasis in adults. Thorax [Internet]. 2019
2534 Jan;74(Suppl 1):1–69. Available from: <http://dx.doi.org/10.1136/thoraxjnl-2018-212463>

2535 154. Herrero-Cortina B, Lee AL, Oliveira A, O'Neill B, Jácome C, Dal Corso S, et al.
2536 European Respiratory Society statement on airway clearance techniques in adults with
2537 bronchiectasis. Eur Respir J [Internet]. 2023 Jul;62(1). Available from:
2538 <http://dx.doi.org/10.1183/13993003.02053-2022>

2539 155. Flume PA, Robinson KA, O'Sullivan BP, Finder JD, Vender RL, Willey-Courand
2540 DB, et al. Cystic fibrosis pulmonary guidelines: airway clearance therapies. Respir Care

2541 [Internet]. 2009 Apr;54(4):522–37. Available from:
 2542 <https://journals.sagepub.com/doi/10.4187/respcare.09540522>

2543 156. Chalmers JD, Haworth CS, Flume P, Long MB, Burgel PR, Dimakou K, et al.
 2544 European Respiratory Society clinical practice guideline for the management of adult
 2545 bronchiectasis. Eur Respir J [Internet]. 2025 Dec;66(6). Available from:
 2546 <http://dx.doi.org/10.1183/13993003.01126-2025>

2547 157. Brackett H, Forman A, Foster LA, Fischer SM. Compassionate Removal of Heated
 2548 High-Flow Nasal Cannula for End of Life: Case Series and Protocol Development. J
 2549 Hosp Palliat Nurs [Internet]. 2021 Aug 1;23(4):360–6. Available from:
 2550 <http://dx.doi.org/10.1097/NJH.0000000000000769>

2551 158. Truog RD, Campbell ML, Curtis JR, Haas CE, Luce JM, Rubenfeld GD, et al.
 2552 Recommendations for end-of-life care in the intensive care unit: a consensus statement
 2553 by the American College [corrected] of Critical Care Medicine. Crit Care Med [Internet].
 2554 2008 Mar;36(3):953–63. Available from:
 2555 <http://dx.doi.org/10.1097/CCM.0B013E3181659096>

2556 159. Wenzel D, Jefferies T, Davies R, Creese J, Wilson E, Faull C. National review of
 2557 end-of-life care withdrawal guidelines for non-invasive advanced respiratory support
 2558 using document analysis. BMJ Open [Internet]. 2024 Oct 15;14(10):e089617. Available
 2559 from: <http://dx.doi.org/10.1136/bmjopen-2024-089617>

2560 160. General Medical Council. Treatment and care towards the end of life: good
 2561 practice in decision making [Internet]. 2024 Dec. Available from: [https://www.gmc-](https://www.gmc-uk.org/professional-standards/the-professional-standards/treatment-and-care-towards-the-end-of-life)
 2562 [uk.org/professional-standards/the-professional-standards/treatment-and-care-towards-](https://www.gmc-uk.org/professional-standards/the-professional-standards/treatment-and-care-towards-the-end-of-life)
 2563 [the-end-of-life](https://www.gmc-uk.org/professional-standards/the-professional-standards/treatment-and-care-towards-the-end-of-life)

2564 161. Mental Capacity Act 2005 [Internet]. UK Public General Act Apr 7, 2005. Available
 2565 from: <https://www.legislation.gov.uk/ukpga/2005/9/contents>

2566 162. Mental Capacity Act Code of Practice [Internet]. GOV.UK. 2013 [cited 2026 Aug
 2567 24]. Available from: [https://www.gov.uk/government/publications/mental-capacity-act-](https://www.gov.uk/government/publications/mental-capacity-act-code-of-practice)
 2568 [code-of-practice](https://www.gov.uk/government/publications/mental-capacity-act-code-of-practice)

2569 163. Ruangsomboon O, Dorongthom T, Chakorn T, Monsomboon A, Praphruekit N,
 2570 Limswat C, et al. High-Flow Nasal Cannula Versus Conventional Oxygen Therapy in
 2571 Relieving Dyspnea in Emergency Palliative Patients With Do-Not-Intubate Status: A
 2572 Randomized Crossover Study. Ann Emerg Med [Internet]. 2020 May;75(5):615–26.
 2573 Available from: <http://dx.doi.org/10.1016/j.annemergmed.2019.09.009>

2574 164. Kim JS, Shin J, Kim NH, Lee SY, Yoo SH, Keam B, et al. Use of high-flow nasal
 2575 cannula oxygen therapy for patients with terminal cancer at the end of life. Cancer Med
 2576 [Internet]. 2023 Jul;12(13):14612–22. Available from:
 2577 <http://dx.doi.org/10.1002/cam4.6060>

2578 165. Bramati PS, Azhar A, Khan R, Tovbin M, Cooper A, Pangemanan I, et al. High
 2579 Flow Nasal Cannula in Patients With Cancer at the End of Life. J Pain Symptom
 2580 Manage [Internet]. 2023 Apr;65(4):e369–73. Available from:
 2581 <http://dx.doi.org/10.1016/j.jpainsymman.2022.12.141>

2582 166. National Institute for Health and Care Excellence. Care of dying adults in the last
2583 days of life (NICE guideline NG31) [Internet]. NICE; 2015 [cited 2026 Aug 24]. Available
2584 from: <https://www.nice.org.uk/guidance/ng31/chapter/Recommendations>

2585 167. Mahler DA, Selecky PA, Harrod CG, Benditt JO, Carrieri-Kohlman V, Curtis JR, et
2586 al. American College of Chest Physicians consensus statement on the management of
2587 dyspnea in patients with advanced lung or heart disease. Chest [Internet]. 2010
2588 Mar;137(3):674–91. Available from: <http://dx.doi.org/10.1378/chest.09-1543>

2589 168. Maddocks M, Lovell N, Booth S, Man WDC, Higginson IJ. Palliative care and
2590 management of troublesome symptoms for people with chronic obstructive pulmonary
2591 disease. Lancet [Internet]. 2017 Sep 2;390(10098):988–1002. Available from:
2592 [http://dx.doi.org/10.1016/S0140-6736\(17\)32127-X](http://dx.doi.org/10.1016/S0140-6736(17)32127-X)

2593