The Danish respiratory society guideline for long-term high flow nasal cannula treatment, with or without supplementary oxygen

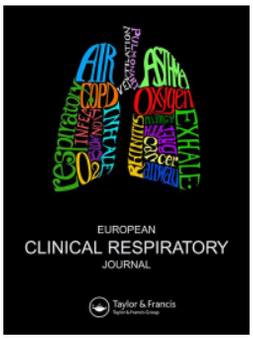
Weinreich, Ulla Møller; Juhl, Kasper Svendsen; Søby Christophersen, Malene; Gundestrup, Svend; Hanifa, Munsoor Ali; Jensen, Kristine; Andersen, Frank Dyekjær; Hilberg, Ole; Storgaard, Line Hust

Published in:
European Clinical Respiratory Journal

DOI:
10.1080/20018525.2023.2178600

Publication date:
2023

Document version:
Final published version



European Clinical Respiratory Journal

ISSN: (Print) (Online) Journal homepage: https://www.tandfonline.com/loi/zecr20

The Danish respiratory society guideline for long-term high flow nasal cannula treatment, with or without supplementary oxygen

Ulla Møller Weinreich, Kasper Svendsen Juhl, Malene Søby Christophersen, Svend Gundestrup, Munsoor Ali Hanifa, Kristine Jensen, Frank Dyekjær Andersen, Ole Hilberg & Line Hust Storgaard

To cite this article: Ulla Møller Weinreich, Kasper Svendsen Juhl, Malene Søby Christophersen, Svend Gundestrup, Munsoor Ali Hanifa, Kristine Jensen, Frank Dyekjær Andersen, Ole Hilberg & Line Hust Storgaard (2023) The Danish respiratory society guideline for long-term high flow nasal cannula treatment, with or without supplementary oxygen, European Clinical Respiratory Journal, 10:1, 2178600, DOI: 10.1080/20018525.2023.2178600

To link to this article: https://doi.org/10.1080/20018525.2023.2178600

EUROPEAN CLINICAL RESPIRATORY JOURNAL
2023, VOL. 10, 2178600
https://doi.org/10.1080/20018525.2023.2178600

Taylor & Francis
Taylor & Francis Group

SHORT COMMUNICATION

OPEN ACCESS Check for updates

The Danish respiratory society guideline for long-term high flow nasal cannula treatment, with or without supplementary oxygen

Ulla Møller Weinreich [a,b], Kasper Svendsen Juhl[a], Malene Søby Christophersen[c], Svend Gundestrup[d], Munsoor Ali Hanifa[e], Kristine Jensen[f], Frank Dyekjær Andersen[g], Ole Hilberg[h] and Line Hust Storgaard[a]

[a]Department of Respiratory Diseases, Aalborg University Hospital, Aalborg, Denmark; [b]The Clinical Department, Aalborg University, Aalborg, Denmark; [c]Department of Emergency Medicine, Horsens Regional Hospital, Horsens, Denmark; [d]Department of Internal Medicine, Rigshospitalet Glostrup, Glostrup, Denmark; [e]Department of Anaesthesia and Intensive Care Medicine, Aalborg University Hospital, Aalborg, Denmark; [f]Department of Cardiology, Copenhagen University Hospital Rigshospitalet, Copenhagen, Denmark; [g]The Diagnostics Center, Silkeborg Regional Hospital, Silkeborg, Denmark; [h]Department of Medicine, Vejle Hospital, Southern Danish University Hospital, Vejle, Denmark

ABSTRACT

Introduction: Long-term High Flow Nasal Cannula (LT-HFNC), defined as High Flow Nasal Cannula treatment provided to patients with chronic pulmonary conditions during stable phases, has emerged as a home treatment in different categories of patients with chronic lung diseases in recent years.

Methods: This paper summarizes the physiological effects of LT-HFNC and evaluates the clinical knowledge to date about treatment in patients with chronic obstructive lung disease, interstitial lung disease and bronchiectasis. The guideline is translated and summarized in this paper and presented unabridged as an appendix to the paper.

Results: The paper describes the working process behind the Danish Respiratory Society's National guideline for treatment of stable disease, which has been written to support clinicians in both evidence-based decision making and practical issues concerning the treatment.

ARTICLE HISTORY
Received 17 October 2022
Accepted 6 February 2023

KEYWORDS
High Flow Nasal Cannula; High flow nasal oxygen; High flow oxygen therapy; Nasal high flow; HFNC; HFNO; HFOT; NHF; long-term treatment; home treatment; Chronic obstructive lung disease; COPD; Interstitial lung disease; ILD; Bronchiectasis

Background

Over the past two decades, the literature on long-term High Flow Nasal Cannula (LT-HFNC), defined as High Flow Nasal Cannula treatment provided to patients with chronic pulmonary conditions during stable phases, has increased considerably [1–3]. Most studies have been conducted in the treatment of patients with Chronic obstructive pulmonary disease (COPD), but studies have also investigated the effect of long-term home treatment in patients with interstitial lung disease and bronchiectasis. In COPD and interstitial lung disease, the target populations have been patients with persistent respiratory failure.

In the paper below, the authors summarize the literature that, after thorough review of the existing literature on physiological and clinical effects in stable chronic respiratory disease, was chosen as the background for the Danish National Guideline for LT-HFNC treatment.

Physiological effects

The physiological effects of High Flow Nasal Cannula have primarily been studied during short-term use of the device, however, the physiological effects of LT-HFNC are expected to be similar, although in some instances with varying importance, to those seen in acute use [4]. The most important are mentioned below.

Mucociliary clearance

Humidification of the airways is essential for a number of reasons. Firstly, patients using long-term oxygen therapy frequently experience dryness of the airways and congestion [5], which has been found to increase airway resistance and increase the work of breathing [6]. Humidification of the airway is also important for airway resistance to inflammation and infection [7,8], and improves the velocity of mucociliary transport [9]. This, alongside the ventilatory mechanisms described below, leads to improved alveolar recruitment [10].

By delivering humidified and heated air, High Flow Nasal Cannula has been shown to improve the mucociliary clearance [11–13]. A temperature and humidity matching human physiology (100%/37°Celsius) will provide the best conditions for mucociliary clearance [14], as ciliary beating has optimal performance at full

CONTACT Ulla Møller Weinreich ulw@rn.dk Department of Respiratory Diseases, Aalborg University Hospital, Mølleparkvej 4, DK-9000 Aalborg Denmark.

Supplemental data for this article can be accessed online at https://doi.org/10.1080/20018525.2023.2178600

humidification [15,16], which should therefore be the target for LT-HFNC treatment.

Anatomical dead space wash-out

High Flow Nasal Cannula treatment increases the wash-out of carbon dioxide (CO_2) from the anatomical dead space [17]. The effect is proportional to the flow, and thereby the decrease in reduction of CO_2 rebreathing [18]. Although the physiological effect on acute hypercapnic failure in COPD is much debated, recent papers do indicate that this may be of use to chronic hypercapnic patients, as short-term use led to reduction, and long-term use to stabilization, of $PaCO_2$ in COPD [19,20]. In addition, the oxygen deposited in the anatomical dead space may also contribute to stabilize oxygen saturation in these respiratorily challenged patient groups [21]. It has been speculated, based on the lack of effect on work of breathing in patients who are treated with High Flow through tracheostomies, that the effect on the work of breathing is mediated through changes in the upper airways [22]. However, this needs further investigation.

Work of breathing

High Flow Nasal Cannula treatment has been shown to reduce the trans-diaphragmatic pressure, the measure of inspiratory effort and the work load of breathing [23,24]. Although the positive end-expiratory pressure effect of High Flow Nasal Cannula is minimal [25], it adequately counteracts hyperinflation in patients with COPD and thereby also decreases the expiratory work load [4,24]. Additionally, the improved ventilation also adds to the stabilization of oxygenation [23], driven by changes in anatomical dead space and alveolar recruitment, described above [10,21]. The optimal flow in the individual patient is closely related to the patients' work of breathing, which has been primarily investigated in patients who are not spontaneously breathing [26]. Whereas the optimal wash out of the anatomical dead space in patients with acute respiratory failure is best obtained with high flows, studies suggest that due to the lower work of breathing, it is better obtained with lower flows in patients with chronic respiratory failure [27–29]. Although not fully understood, this is, through technical models, explained by more optimal conditions for exhalation at lower flows [30].

Domiciliary high flow nasal cannula – current knowledge

Only in recent years has High Flow Nasal Cannula moved out of the hospital and into patients' homes. Most studies have been conducted in patients with COPD; studies in patients with bronchiectasis and interstitial lung disease are sparse.

Long term high flow nasal cannula in COPD

Most studies of the effect of LT-HFNC have been conducted in patients with COPD with persistent hypoxic failure. A study by Nagata et al found improved health-related quality of life in a 6-week cross-over study [25]. A recent feasibility study also showed improved health-related quality of life in patients with COPD treated with High Flow Nasal Cannula after COPD exacerbations requiring hospitalization [31]. D'Cruz et al found reduced symptoms, judged by the COPD assessment test, and a significantly lower 30-day readmission rate in a similar feasibility study [3]. A qualitative study by Storgaard et al found patient-perceived reductions in symptoms [32]. In a 12-month observational study by Rea et al, in a mixed population of patients with respiratory diseases, half with COPD, patients had a prolonged time to first acute exacerbation of COPD, a shorter duration of exacerbations, as well as a significant improvement in forced expiratory volume in the first second (FEV1), despite usage of less than two hours per day [33]. In a 12-month randomized controlled trial, including 200 patients with stable COPD and persistent respiratory failure (randomized equally to recommended therapy or recommended therapy plus LT-HFNC), Storgaard et al found several significant differences compared to a control group: a reduction in acute exacerbations of COPD; reduction in hospitalizations, when corrected for time of use; reduced dyspnea; and preserved walking distance, FEV1 and health-related quality of life [34]. A later sub-study revealed the effect on exacerbations and hospitalizations to be primarily for patients with frequent acute exacerbations of COPD (≥2 per 12 months) [35]. A number of studies have shown improved exercise performance [33,36,37]. In a qualitative study from Storgaard et al, a reduction in night-time symptoms was a very consistent finding from all participating patients [32]. Although LT-HFNC has primarily been targeted to persistent hypoxic failure, a number of studies have also reported an effect on persistent hypercapnia. Both Pisani et al and Brâunlich et al found, in a comparison between non-invasive ventilation (NIV) and High Flow Nasal Cannula on $PaCO_2$-levels, that there were no significant differences in $PaCO_2$ levels following NIV or LT-HFNC treatment [19,38]. Both Nagata et al and Storgaard et al found that $PaCO_2$ remained stable in patients treated with

LT-HFNC, which was significantly different from controls, whose $PaCO_2$ increased. Furthermore, both studies found a significant reduction in exacerbations in the HFNC treated group [39,40]. Three studies have indicated that LT-HFNC treatment is cost-effective [41–43].

In study settings, treatment has been well tolerated; however, D'Cruz et al found that 83% completed the first month [3], and Storgaard et al also found drop-out to be most pronounced in the first month [44]. The drop out is comparable to that seen in patients treated with LT-NIV [45]. Furthermore, an abstract on a post-trial analysis of the Danish cohort showed that most patients used LT-HFNC until time of death [44]. Lastly, higher flows have been associated with lower adherence [46]. In summary, a number of authors have found that LT-HFNC reduces number- and increase time to next exacerbation; reduces dyspnea, and there are indications of a stabilizing effect for patients with COPD and stable hypercapnic failure on $PaCO_2$-levels and number of exacerbations.

Long term high flow nasal cannula in bronchiectasis

Literature on LT- HFNC treatment in patients with bronchiectasis is sparse. More than a decade ago, Hasani et al showed that mucociliary clearance improved in patients with bronchiectasis after only seven-days treatment [8]. Recently, a subgroup analysis was published on the 12-month randomized controlled trial by Rea et al [33], investigating the 45 patients with bronchiectasis from the original cohort of patients with obstructive lung diseases. The study found that patients had a reduction in acute exacerbations of bronchiectasis and improved health-related quality of life [47]. One large randomized controlled trial is ongoing, investigating the effect of High Flow Nasal Cannula on health-related quality of life in bronchiectasis (ClinicalTrial.gov NCT04142827); recruitment status is unknown. Otherwise, literature consists of case reports at present [48].

In summary, literature is sparse in LT-HFNC treatment of patients with bronchiectasis, but there are indications of a reduction in number of exacerbations.

Long term high flow nasal cannula in interstitial lung disease

As in bronchiectasis, the literature on LT-HFNC use in interstitial lung disease is sparse. Bräunlich et al have shown that LT-HFNC reduced respiratory rate in patients with interstitial lung disease [49]. Chikhanie et al found LT-HFNC to increase both endurance and exercise tolerance in interstitial lung disease, and to reduce leg fatigue, which was consistent with the findings of Suzuki et al, who also found LT-HFNC to improve endurance [50]. Huremovic et al found improved walking distance and reduced time to oxygen saturation recovery [51]. All aforementioned studies found the effect of LT-HFNC to be highly variable in between individual patients. A single abstract suggests improved recovery, in terms of endurance, after an acute exacerbation of interstitial lung disease [52].

In summary, studies on LT-HFNC treatment in patients with interstitial lung disease are few, but there are indications of an effect on exercise tolerance.

Based on the clinical and physiological evidence available for LT-HFNC, the Danish Respiratory Society decided to make a clinical guideline for the use of LT-HFNC treatment in stable phase in 2019. The guideline has been updated in 2022 [53].

Methods

The Danish Respiratory Society guidelines are short and operational clinical guidelines based on the principles of the National Institute for Health and Care Excellence [54].

A background literature search was performed in PubMed, Embase and on Google Scholar; as there are no established Mesh- and Emtree terms for HFNC, the searches were performed as free text searches. Three literature searches were performed, utilizing 'High Flow' OR 'High Flow Nasal Cannula' OR 'HFNC' OR 'High Flow nasal oxygen' OR 'HFNO' OR "Nasal High Flow"OR 'NHF' OR 'High Flow Oxygen Therapy' OR 'HFOT' in connection with the specific lung diseases: 'COPD' OR 'Chronic Obstructive Lung Disease' OR 'Chronic Obstructive Pulmonary Disease'; 'Interstitial lung disease' OR 'ILD'; and 'Bronchiectasis', respectively.

The initial guideline was based on a workshop, where the authors of the guideline discussed the available literature and knowledge of LT-HFNC use, to set the outline of the guideline. The revision was based on the literature published since 2019, on the physiological knowledge about High Flow Nasal Cannula and LT-HFNC clinical outcomes. Furthermore, the group behind the guideline had made themselves available to the Danish Respiratory Community for questions about the guideline and LT-HFNC in general, and the reflections on implementation were recorded and used in the revision of the guideline.

The Danish Guideline was translated from Danish to English by forth-back translation: two of the participating authors of the Danish version translated the

guideline to English, compared translations and agreed on a proposed English version. Hereafter, the guideline was back-translated by a bilingual third person not affiliated to the work, and the original Danish version and the back-translation were compared. Minor changes to the original English translation were made, based on this.

Results

The Danish Respiratory Society guideline recommends use of LT-HFNC in patients with COPD with frequent acute exacerbations of COPD (≥two severe acute exacerbations of COPD per year) and persistent hypoxic respiratory failure, defined according to Danish Respiratory Society guidelines as PaO_2 (without supplementary oxygen treatment) ≤7.3 kPa in clinically stable conditions, including optimized COPD treatment regimens, or PaO_2 (without supplementary oxygen treatment) ≤ 8.0 kPa in case of concomitant right sided heart failure or haematocrit>55% [55]. Furthermore, LT-HFNC is recommended for patients with COPD who are difficult to wean from High Flow Nasal Cannula treatment after an acute exacerbation of COPD. In addition to this, LT-HFNC may be considered for the treatment of patients with interstitial lung disease and persistent hypoxic failure, and patients with severe bronchiectasis, both with- and without persistent hypoxic failure, with frequent acute exacerbations of bronchiectasis. Lastly, LT-HFNC may be considered for patients with COPD with persistent hypercapnic failure, to whom long term NIV is recommended, according to Danish Respiratory Society guidelines (persistent stable hypercapnia, $paCO_2$≥7 kPa, 2–4 weeks after NIV-treated acute exacerbation of COPD and > three NIV treated acute exacerbations of COPD, in addition to patients who cannot be weaned after NIV treated acute exacerbation of COPD) [56], but who do not tolerate long term NIV.

It is recommended to treat patients with a flow of 15–35 L/min, depending on the patients' respiratory work. Higher flows of up to 40 L/min should only be considered for patients with a high respiratory rate or a large respiratory workload, based on clinical evaluation. Hereafter, a target saturation is set, and based on this, the FiO_2 is titrated in order to reach the target saturation. A daily use of 6–8 hours is recommended, and in order to keep patients as physically active as possible, the guideline suggests night-time use. A temperature of 37°Celsius is recommended. Both flow and temperature may be titrated towards the target over a longer period of time.

The full version of the translated guideline is available in Supplementary material.

Discussion

The Danish Respiratory Society Guideline for LT-HFNC is the first guideline in this area in the world.

Although guidelines and reviews have recommended the use of High Flow Nasal Cannula in an acute setting [57,58], previous reviews have concluded that more evidence was needed before LT-HFNC could be incorporated into clinical practice in the treatment of patients with chronic lung disease in stable phases [46,59]. LT-HFNC has been evaluated in different institutions. Although not recommended for patients with COPD and persistent hypoxic failure by the German Institute for Quality and Efficiency in Health Care [59], German insurance companies do re-imburse LT-HFNC costs to patients who do not tolerate long-term NIV, despite the lack of literature on the area [60]. Therefore, there may be those who question why the Danish Respiratory Society chose to make a national guideline. There are several reasons why we chose to make this guideline. Firstly, the treatment is used throughout the country for treatment of persistent hypoxic failure, with no real contraindications apart from poor adherence to therapy, and it is desirable that health care professionals are aware of the level of evidence on which they base their clinical choices. Secondly, to give clinicians who wish to use LT-HFNC a clear understanding of the fact that acute- and long-term use of High Flow Nasal Cannula are not the same. Thirdly, when used, it is important that the treatment is used correctly for patients to get optimal treatment, and for clinicians to evaluate the effect of LT-HFNC on a sound basis. And lastly, by aligning treatment throughout the country, we hope to improve the validity of real-life data, which could be used for quality control and scientific purposes in the future.

The guideline recommends treatment for patients with COPD and bronchiectasis with exacerbations, although evidence is limited. The post hoc analysis by Weinreich of the Danish randomized controlled trial of patients with COPD indicates that the effect of LT-HFNC on exacerbations is primarily seen in patients with previous exacerbations [35]. Similarly, the post hoc analysis of the study by Rea et al also indicates that the effect is primarily seen in patients with exacerbations. Recently, studies by Nagata and Crimi et al, not published when the Danish guideline was reviewed, support the use of LT-HFNC in COPD and bronchiectasis with exacerbations [39,40]. Despite this, it is important to remember that the effect on dyspnea has

been convincing in both COPD, bronchiectasis, and interstitial lung diseases. Therefore, dyspnea could also be an indication for LT-HFNC treatment.

The Danish Respiratory Society guideline is, of course, targeted to Danish respiratory physicians. There may be numerous differences in practical and logistical matters that make the guideline not directly applicable for colleagues in other countries. Furthermore, the guideline refers to other Danish guidelines, which may not apply to other countries' settings. When we choose to publish the guideline in an English version, as a direct translation of the Danish version, it is to offer inspiration to colleagues around the world, and to offer a guide to the hands-on use of LT-HFNC.

Do we need more data on LT-HFNC? Of that there is no doubt. In both interstitial lung disease and bronchiectasis, data are limited, and studies are needed in every aspect of LT-HFNC treatment, be it target population, treatment effect or health-economic evaluation. In COPD, confirmatory studies are needed to further establish the target population for LT-HFNC treatment, and to investigate the role and the effect of LT-HFNC in persistent hypercapnic failure. The optimal flow is not established; lower flows will probably improve adherence and mechanical models suggest better airway clearance at lower flows – however, no studies on higher flows in stable conditions exist. The optimal duration of use has not been investigated in any of the chronic diseases, and it is therefore not known whether it differs between diseases; the most common recommended time of use in the different studies has therefore been applied in the guideline. Therefore, the Danish Respiratory Society guideline will also need frequent updates in years to come, and there is a hypothetical risk that conclusions may change considerably over time.

In conclusion, evidence about the use of LT-HFNC treatment in stable chronic respiratory disease is emerging, and there are strong indications of the treatment being useful in patients with COPD and bronchiectasis with recurrent exacerbations, as well as in patients with interstitial lung diseases for improving physical performance. The Danish Respiratory Society guideline for LT-HFNC treatment is a proposal to help clinicians make evidence-based decisions regarding treatment; to give the users hands-on guidance in the use of the device; to ensure that patients treated with LT-HFNC are treated correctly, based on current knowledge; and to build a platform for national evaluation of treatment.

Disclosure statement

Line Hust Storgaard has received funding for research and speaker's fees from Fisher&Paykel Healthcare, and speaker's fees from ResMed.Ulla Møller Weinreich has received funding for research and speaker's fees from Fisher&Paykel Healthcare, and speaker's fees and fees for advisory board participation from ResMed.

Funding

This paper has not received any funding.

ORCID

Ulla Møller Weinreich http://orcid.org/0000-0003-1975-3654

References

[1] Li J, Jing G, Scott JB. Year in review 2019: high-flow nasal cannula oxygen therapy for adult subjects. Respir Care. 2020;65(4):545–557.

[2] Salvador D-L, José Manuel Carratalá P, Jose Miguel Alonso I, et al. Things to keep in mind in high flow therapy: as usual the devil is in the detail. Int J Crit Care Emerg Med. 2018;4(2):1–8. DOI:10.23937/2474-3674/1510048

[3] D'cruz R, Rossel A, Suh ES, et al. Home nasal high-flow following severe COPD exacerbation: a mixed-methods feasibility randomised controlled trial. Eur Respir J. 2021;58:OA1626.

[4] D'cruz RF, Hart N, Kaltsakas G. High-flow therapy: physiological effects and clinical applications educational aims provide a practical guide to HFT setup and delivery. Outline the physiological effects of HFT on the respiratory system. Breathe. 2020;16:1–10.

[5] Björklund F, Ekström M. Adverse effects, smoking, alcohol consumption, and quality of life during long-term oxygen therapy: a nationwide study. Ann Am Thorac Soc. 2022;19(10):1677–1686.

[6] Fontanari P, Zattara-Hartmann MC, Burnet H, et al. Nasal eupnoeic inhalation of cold, dry air increases airway resistance in asthmatic patients. Eur Respir J. 1997;10(10):2250–2254.

[7] Jiang M, Song JJ, Guo XL, et al. Airway humidification reduces the inflammatory response during mechanical ventilation. Respir Care. 2015;60(12):1720–1728.

[8] Hasani A, Chapman TH, McCool D, et al. Domiciliary humidification improves lung mucociliary clearance in patients with bronchiectasis. Chron Respir Dis. 2008;5(2):81–86. DOI:10.1177/1479972307087190

[9] Kelly SJ, Brodecky V, Skuza EM, et al. Variability in tracheal mucociliary transport is not controlled by beating cilia in lambs in vivo during ventilation with humidified and nonhumidified air. Am J Physiol - Lung Cell Mol Physiol. 2021;320(4):L473–485.

[10] Artaud-Macari E, Bubenheim M, Le Bouar G, et al. High-flow oxygen therapy versus noninvasive ventilation: a randomised physiological crossover study of alveolar recruitment in acute respiratory failure. ERJ Open Res. 2021;7(4):00373–2021. DOI:10.1183/23120541.00373-2021

[11] Chikata Y, Izawa M, Okuda N, et al. Humidification performance of two high-flow nasal cannula devices: a bench study. Respir Care. 2014;59(8):1186–1190. DOI:10.4187/respcare.02932

[12] Koyauchi T, Hasegawa H, Kanata K, et al. Efficacy and tolerability of high-flow nasal cannula oxygen therapy for hypoxemic respiratory failure in patients with interstitial lung disease with do-not-intubate orders: a retrospective single-center study. Respiration. 2018;96(4):323–329. DOI:10.1159/000489890

[13] Chikata Y, Morinishi K, Nishimura M. Humidification in very-high-flow nasal-cannula therapy in an adult lung model. Respir Care. 2019;64(7):809–817.

[14] Spicuzza L, Schisano M. High-flow nasal cannula oxygen therapy as an emerging option for respiratory failure: the present and the future. Ther Adv Chronic Dis. 2020;11:1–15.

[15] Kilgour E, Rankin N, Ryan S, et al. Mucociliary function deteriorates in the clinical range of inspired air temperature and humidity. Intensive care Med. 2004;30 (7):1491–1494.

[16] Plotnikow GA, Accoce M, Navarro E, et al. Humidification and heating of inhaled gas in patients with artificial airway. A narrative review. Rev Bras Ter Intensiva. 2018;30(1):86–97.

[17] Möller W, Feng S, Domanski U, et al. Nasal high flow reduces dead space. J Appl Physiol. 2017;122 (1):191–197. DOI:10.1152/japplphysiol.00584.2016

[18] Möller W, Celik G, Feng S, et al. Nasal high flow clears anatomical dead space in upper airway models. J Appl Physiol. 2015;118(12):1525–1532. DOI:10.1152/japplphysiol.00934.2014

[19] Pisani L, Betti S, Biglia C, et al. Effects of high-flow nasal cannula in patients with persistent hypercapnia after an acute COPD exacerbation: a prospective pilot study. BMC Pulm Med. 2020;20(1):1–9. DOI:10.1186/s12890-020-1048-7

[20] Storgaard LH, Hockey HU, Weinreich UM. Development in PaCO 2 over 12 months in patients with COPD with persistent hypercapnic respiratory failure treated with high-flow nasal cannula—post-hoc analysis from a randomised controlled trial. BMJ Open Respir Res. 2020;7(1):10–14.

[21] Wettstein RB, Shelledy DC, Peters JI. Delivered oxygen concentrations using low-flow and high-flow nasal cannulas. Respir Care. 2005;50(5):604–609.

[22] Stripoli T, Spadaro S, Di Mussi R, et al. High-flow oxygen therapy in tracheostomized patients at high risk of weaning failure. Ann Intensive Care. 2019;9(1). DOI:10.1186/s13613-019-0482-2

[23] Mauri T, Turrini C, Eronia N, et al. Physiologic effects of high-flow nasal cannula in acute hypoxemic respiratory failure. Am J Respir Crit Care Med. 2017;195 (9):1207–1215. DOI:10.1164/rccm.201605-0916OC

[24] Pisani L, Vega ML. Use of nasal high flow in stable COPD: rationale and physiology. COPD J Chronic Obstr Pulm Dis. 2017;14(3):346–350.

[25] Nagata K, Kikuchi T, Horie T, et al. Domiciliary high-flow nasal cannula oxygen therapy for patients with stable hypercapnic chronic obstructive pulmonary disease. a multicenter randomized crossover trial. Ann Am Thorac Soc. 2018;15(4):432–439. DOI:10.1513/AnnalsATS.201706-425OC

[26] Fricke K, Schneider H, Biselli P, et al. Nasal high flow, but not supplemental O2, reduces peripheral vascular sympathetic activity during sleep in COPD patients. 2018;13:3635–3643.

[27] Biselli PJC, Kirkness JP, Grote L, et al. Nasal high-flow therapy reduces work of breathing compared with oxygen during sleep in COPD and smoking controls: a prospective observational study. J Appl Physiol. 2017;122(1):82. DOI:10.1152/japplphysiol.00279.2016

[28] Dysart K, Miller TL, Wolfson MR, et al. Research in high flow therapy: mechanisms of action. Respir med. 2009;103(10):1400–1405.

[29] Di Mussi R, Spadaro S, Stripoli T, et al. High-flow nasal cannula oxygen therapy decreases postextubation neuroventilatory drive and work of breathing in patients with chronic obstructive pulmonary disease. crit care. 2018;22(1):1–11. DOI:10.1186/s13054-018-2107-9

[30] Onodera Y, Akimoto R, Suzuki H, et al. A high-flow nasal cannula system set at relatively low flow effectively washes out CO2 from the anatomical dead space of a respiratory-system model. Korean J Anesthesiol. 2017;70 (1):105–106.

[31] Criner GJ, Criner LH, George CRNSA, et al. Chronic obstructive pulmonary diseases: feasibility of using daily home high-flow nasal therapy in COPD patients following a recent COPD hospitalization. Chronic Obstr Pulm Dis. 2022;9(1):4–14.

[32] Storgaard LH, Weinreich UM, Laursen BS. COPD patients' experience of long-term domestic oxygen-enriched nasal high flow treatment: a qualitative study. COPD. 2020;17(2):175–183.

[33] Rea H, McAuley S, Jayaram L, et al. The clinical utility of long-term humidification therapy in chronic airway disease. Respir med. 2010;104(4):525–533. DOI:10.1016/j.rmed.2009.12.016

[34] Storgaard LH, Hockey H, Laursen BS, et al. Long-term effects of oxygen-enriched nasal high flow treatment in COPD with chronic hypoxemic respiratory failure. 2018;13:1195–1205.

[35] Weinreich UM, Kou YR. Domiciliary high-flow treatment in patients with COPD and chronic hypoxic failure: in whom can we reduce exacerbations and hospitalizations? PLoS ONE. 2019;14(12):e0227221.

[36] Chatila W, Nugent T, Vance G, et al. The effects of high-flow vs low-flow oxygen on exercise in advanced obstructive airways disease. Chest. 2004;126:1108–1115.

[37] Cirio S, Piran M, Vitacca M, et al. Effects of heated and humidified high flow gases during high-intensity constant-load exercise on severe COPD patients with ventilatory limitation. Respir med. 2016;118:128–132.

[38] Bräunlich J, Dellweg D, Bastian A, et al. nasal high-flow versus noninvasive ventilation in patients with chronic hypercapnic COPD. 2019;14:1411–1421.

[39] Nagata K, Horie T, Chohnabayashi N, et al. Home high-flow nasal cannula oxygen therapy for stable hypercapnic COPD: a randomized clinical trial. Am J Respir Crit Care Med. 2022;206(11):1326–1335. DOI:10.1164/rccm.202201-0199OC

[40] Crimi C, Nolasco S, Campisi R, et al. Long-term domiciliary high-flow nasal therapy in patients with bronchiectasis: a preliminary retrospective observational case-control study. J Clin Med. 2022;11(24):1–16. DOI:10.3390/jcm11247323

[41] Milne RJ, Hockey H, Rea H. Long-term air humidification therapy is cost-effective for patients with moderate or severe chronic obstructive pulmonary disease or bronchiectasis. Value Heal. 2014;17(4):320–327.

[42] Sørensen SS, Weinreich UM, Storgaard LH. Assessment of health-related quality of life and hospital admission costs of domiciliary high-flow nasal cannula treatment for severe COPD with chronic hypoxic failure. Eur Respir J. 2020;56:1661.

[43] Milne RJ, Garrett J, Garrett J. Hospital cost savings for sequential COPD patients receiving domiciliary nasal high flow therapy. 2022;Volume 17:1311–1322.

[44] Storgaard L, Weinreich UM. Follow up after end of trial: evaluation of usage of oxygen-enriched nasal high flow treatment in COPD with chronic hypoxemic respiratory failure. Clinical ProblemsVol. A693. European Respiratory Society. 2018. 10.1183/13993003.congress-2018.PA693

[45] Murphy PB, Rehal S, Arbane G, et al. Effect of home noninvasive ventilation with oxygen therapy vs oxygen therapy alone on hospital readmission or death after an acute COPD exacerbation. JAMA. 2017;317(21):2177. DOI:10.1001/jama.2017.4451

[46] Elshof J, Duiverman ML. Clinical evidence of nasal high-flow therapy in chronic obstructive pulmonary disease patients. Respiration. 2020;99(2):140–153.

[47] Good WR, Garrett J, Hockey HUP, et al. The role of high-flow nasal therapy in bronchiectasis: a post hoc analysis. ERJ Open Res. 2021;7(1):00711–02020. DOI:10.1183/23120541.00711-2020

[48] Impellizzeri P, Nolasco S, Campisi R, et al. Acute and long-term management of severe bronchiectasis with high flow nasal therapy: a case report. Monaldi Arch Chest Dis. 2022. DOI:10.4081/monaldi.2022.2333.

[49] Bräunlich J, Beyer D, Mai D, et al. Effects of nasal high flow on ventilation in volunteers, COPD and idiopathic pulmonary fibrosis patients. Respiration. 2013;85 (4):319–325. DOI:10.1159/000342027

[50] Suzuki A, Ando M, Kimura T, et al. The impact of high-flow nasal cannula oxygen therapy on exercise capacity in fibrotic interstitial lung disease: a proof-of-concept randomized controlled crossover trial. BMC Pulm Med. 2020;20(1):1–10. DOI:10.1186/s12890-020-1093-2

[51] Huremovic J, Burchardt C, Møller Weinreich U. The effect of domiciliary High Flow Nasal Cannula treatment on dyspnea and walking distance in patients with interstitial lung disease – a pilot study has been successfully submitted online and is presently being given full consideration for publication. Chron Respir Dis. 2022. doi:10.1177/14799731221137085.

[52] Arizono S, Oomagari M, Yanagita Y, et al. Benefits of high-flow nasal cannula oxygen therapy on exercise capacity following acute exacerbation in ILD patients. Eur Respir J. 2020;56:A4662.

[53] Juhl KS, Christophersen MS, Gundestrup S, et a. Danish Respiratory Society: High Flow Hjemmebehandling. [accessed 2022 Sep]. lungemedicin.dk.

[54] National Institute for Health and Care Excellence. The guidelines manual : appendix M – Guide to the short clinical guideline process: 2022. [accessed 2022 Sep]. https://www.nice.org.uk.

[55] Ringbæk T, Jensen MS, Løkke A, et al. Danish Respiratory Society: Iltbehandling i hjemmet. [accessed 2022 Sep]. lungemedicin.dk.

[56] Holm CP, Gantzhorn EK, Weinreich UM, et al. Danish Respiratory Society: KOL - LT-NIV (hjemme NIV). [accessed 2022 Sep]. lungemedicin.dk.

[57] Ergan B, Oczkowski S, Rochwerg B, et al. European Respiratory Society Guideline on Long- term Home Non-Invasive Ventilation for Management of Chronic Obstructive Pulmonary Disease. Eur Respir J. 2019;54 (3):1901003. DOI:10.1183/13993003.01003-2019

[58] Oczkowski S, Ergan B, Bos L, et al. ERS clinical practice guidelines: high-flow nasal cannula in acute respiratory failure. Eur Respir J. 2022;59:2101574. DOI:10.1183/13993003.01574-2021.

[59] IQWIG. Self-administered high-flow therapy for COPD and type 1 respiratory failure: benefit not proven. 2021. https://www.iqwig.de/en/presse/press-releases/press-releases-detailpage_42180.html.

[60] Horvath C, Baty F, Kähler C. Long term home high flow nasal cannula therapy in hypercapnic and hypoxic patients after non-invasive ventilation failure – a retrospective analysis. in *Noninvasive ventilatory support* PA4034. European Respiratory Society; 2019. DOI:10.1183/13993003.congress-2019.PA4034.