CHEST

Home Noninvasive Ventilation in COPD

Marta Kaminska, MD; Veronique Adam, RRT; and Jeremy E. Orr, MD

Evidence is increasing that long-term noninvasive ventilation (LTNIV) can improve outcomes in individuals with severe, hypercapnic COPD. Although the evidence remains unclear in some aspects, LTNIV seems to be able to improve patient-related and physiologic outcomes like dyspnea, FEV_1 and partial pressure of carbon dioxide (P_{CO_2}) and also to reduce rehospitalizations and mortality. Efficacy generally is associated with reduction in P_{CO_2}. To achieve this, an adequate interface (mask) is essential, as are appropriate ventilation settings that target the specific respiratory physiologic features of COPD. This will ensure comfort, synchrony, and adherence that will result in physiologic improvements. This article briefly reviews the newest evidence and current guidelines on LTNIV in severe COPD. It describes an actual patient who benefitted from the therapy. Finally, it provides strategies for initiating and optimizing this LTNIV in COPD, discussing high-pressure noninvasive ventilation, optimization of triggering, and control of inspiratory time. As demand increases, clinicians will need to be familiar with this therapy to reap its benefits, because inadequately adjusted LTNIV will not be tolerated or effective.

CHEST 2024; 165(6):1372-1379

KEY WORDS: chronic respiratory failure; COPD; hypoventilation; noninvasive ventilation

COPD is a major cause of morbidity and the third-leading cause of death worldwide.[1] With progressive disease, chronic hypercapnic respiratory failure may occur, which is associated with a 1-year mortality of 17% to 30%.[2-5] Hospitalization resulting from hypercapnic exacerbation is associated with 11% in-hospital mortality and 49% 2-year mortality.[6]

The benefits of noninvasive ventilation (NIV) in acute exacerbations are well established.[7-10] For chronic use in the home setting, older systematic reviews found no evidence of benefit, but did identify higher baseline CO_2, higher pressures, and longer daily NIV use as predictors of greater CO_2 reduction.[11] Recent randomized controlled trials have changed the landscape in the field. However, practice had been variable, from higher proportions of patients with COPD in ventilation programs in European countries[12-14] to few across Canadian provinces[15] and generally few chronically hypercapnic patients with COPD receiving home NIV in the United States.[16] Hence, experience with long-term NIV (LTNIV) is highly heterogeneous among pulmonologists. Varying ventilation targets,[17] rapid technological advances with

ABBREVIATIONS: ATS = American Thoracic Society; BUR = backup rate; EPAP = expiratory positive airway pressure; IPAP = inspiratory positive airway pressure; LTNIV = long-term noninvasive ventilation; LTOT = long-term oxygen therapy; NIV = noninvasive ventilation; P_{CO_2} = partial pressure of carbon dioxide; P_{VCO_2} = partial pressure of carbon dioxide in venous blood; SpO_2 = hemoglobin oxygen saturation by pulse oximetry; Ti = inspiratory time

AFFILIATIONS: From the Quebec National Program for Home Ventilatory Assistance (M. K. and V. A.), the Division of Respiratory Medicine (M. K.), Department of Medicine, McGill University Health Centre, Montreal, QC, Canada, and the Division of Pulmonary, Critical Care, Sleep Medicine, and Physiology (J. O.), University of California, San Diego, La Jolla, CA.

CORRESPONDENCE TO: Marta Kaminska, MD; email: marta.kaminska@mcgill.ca

DOI: https://doi.org/10.1016/j.chest.2024.01.030

different ventilation modes, diverse settings and nomenclature among manufacturers, and the multitude of parameters on NIV devices resulting in wide range of possible prescriptions all make NIV a complex therapy that may be challenging to implement. The purpose of this review is to summarize the current data and guidelines on LTNIV in COPD and to provide a practical approach to its initiation.

Evidence for LTNIV in COPD

Randomized controlled trials of NIV in COPD published before 2010 largely failed to demonstrate benefits for physiologic, functional, or patient-reported outcomes or reduction of hospitalizations or survival.[11,18] One exception was an Australian trial comparing LTNIV with long-term oxygen therapy (LTOT) or LTOT alone, which found improvement in mortality with LTNIV after a mean follow-up of 2.21 years.[4] However, worsening of certain quality-of-life parameters was observed, which hampered widespread support for LTNIV in COPD.[19]

In parallel, work carried out in Europe generated increasing evidence that LTNIV could result in improved outcomes if settings were adjusted targeting obstructive COPD physiologic features and with specific CO_2 reduction goals, termed *high-intensity ventilation*.[20-22] Although the exact definition of high-intensity NIV remains somewhat contentious, it is primarily the high pressure, rather than a high backup rate, that is the most relevant parameter.[23,24] Using this type of strategy, Kohnlein et al[5] demonstrated markedly improved survival with LTNIV in stable hypercapnic patients with COPD, with improved quality of life. The mean inspiratory positive airway pressure (IPAP) and expiratory positive airway pressure (EPAP) were 21.6 and 4.8 cm H_2O, respectively, with backup rate (BUR) of 16.1/min. This trial included participants with $Paco_2$ of $\geq$ 52 mm Hg (mean, 58 mm Hg) and showed reduction, but not normalization, of daytime $Paco_2$ and improvement in oxygen saturation and FEV_1. Murphy et al[25] studied patients who remained hypercapnic (mean Pco_2, 59 mm Hg) 2 to 4 weeks after hospitalization for exacerbation requiring acute NIV and who met criteria for LTOT. Using mean IPAP and EPAP of 24 and 4 cm H_2O, respectively, they demonstrated delayed time to readmission, reduced readmission rate, and improved quality of life. No improvement in mortality was found, but many control patients eventually crossed over to active treatment, and few deaths occurred. Conversely, another trial also including hypercapnic participants (mean Pco_2, approximately 59 mm Hg) after exacerbation did not demonstrate benefit of NIV on readmissions or death[26] using mean IPAP and EPAP of 19 and 4 cm H_2O, respectively. It has been suggested that this resulted from inclusion of participants randomized as early as 48 h after discontinuation of acute NIV who may not have been chronically hypercapnic, because reduction of Pco_2 in the control group mirrored that in the NIV group in the first 3 months. Variable results across modern trials highlight that LTNIV benefits very specific patient populations with COPD; the trials with positive results define the indications and target populations.

Real-world data, notwithstanding potential biases, have helped us to understand the impact of LTNIV in North America. Retrospective single-center studies demonstrated good adherence,[27] improved event-free survival with LTNIV after discharge,[28] and marked reduction in rehospitalizations with a multimodal intervention including LTNIV.[29] Using Medicare data, it was demonstrated that in patients with COPD and chronic respiratory failure, LTNIV was associated with reduced all-cause mortality, hospitalizations, and ED visits,[30,31] with benefit on mortality and reduction in Medicare expenditures restricted to those with hypercapnia.[16]

Clinical Practice Guidelines

The European Respiratory Society,[32] American Thoracic Society (ATS),[33] and the Canadian Thoracic Society[34] recently published guidelines that agree that a role exists for LTNIV in chronic stable hypercapnic COPD, but recommendations are weak, with very low- to moderate-certainty evidence. LTNIV is suggested after acute hypercapnic respiratory failure requiring acute NIV, provided that the patient remains hypercapnic after resolution of the acute episode. The ATS and Canadian Thoracic Society recommend re-evaluation after 2 to 4 weeks. All three guidelines specify that NIV should aim to normalize or at least significantly reduce hypercapnia. The European Respiratory Society and Canadian Thoracic Society found no evidence to support autoadjusting modes preferentially and recommend fixed pressure modes. The ATS suggests evaluating patients for OSA at a minimum with a questionnaire (very low-certainty evidence). Many unanswered questions remain regarding implementation of LTNIV in COPD, including the need to identify better the patients most likely to benefit, to develop strategies to initiate and optimize LTNIV, and to clarify

management of hypercapnic patients with COPD and obesity, especially given the high obesity rates in North America, including in patients with COPD.[27]

Case Study

A 57-year-old man was referred for optimization of home NIV in December 2021. He had previously smoked (35 pack-years) and had quit 1 year prior, and had a BMI of 25 kg/m^2, FEV_1 of 0.6 L (19% predicted), and was receiving optimal bronchodilator therapy and LTOT. He had undergone multiple hospitalizations for hypercapnic respiratory failure over the 2 years prior, with maximal venous partial pressure of carbon dioxide in venous blood ($PvCO_2$) of 136 mm Hg and requiring NIV acutely several times and intubation once. His arterial blood gas 3 years prior showed pH 7.4 and $PaCO_2$ 59 mm Hg.

This patient likely would have benefitted from earlier implementation of home NIV, which may have prevented rehospitalizations and intubation. He had been started on nocturnal NIV at the referring center using an oronasal mask, in spontaneous-timed mode as per parameters used during his last admission: IPAP, 16 cm H_2O; EPAP, 10 cm H_2O; BUR, 12/min; rise time, 300 ms; inspiratory time (Ti) minimum, 0.8 s; Ti maximum, 1.6 s; high trigger sensitivity; and medium cycling sensitivity. These parameters are not optimal because of low IPAP and low driving pressure (Δ = IPAP – EPAP). It is unclear why the EPAP was relatively high, but this was comfortable for the patient. The rise time should be faster, Ti maximum should be lower, and cycling sensitivity should be high for earlier cycling from IPAP to EPAP (clarified herein).

Despite symptomatic improvement, he was rehospitalized briefly with $PvCO_2$ of 102 mm Hg. On discharge, parameters were modified remotely by his home care respiratory therapist to IPAP of 19 cm H_2O, with fastest rise time. The patient reported good subjective sleep quality with NIV. A few days later, a routine follow-up $PvCO_2$ measurement obtained at home was 119 mm Hg.

The driving pressure remained low in the context of COPD. Note that $PvCO_2$, while convenient, is not recommended because it is not a reliable estimate of $PaCO_2$. IPAP was increased gradually remotely to 25 cm H_2O, with Ti maximum of 1.3 s. About 9 months after starting NIV, an overnight oximetry on NIV and oxygen at 3 L/min showed mean hemoglobin oxygen saturation by pulse oximetry (SpO_2) of 95% and SpO_2 of < 90% during 0.8% of the night. The daytime transcutaneous CO_2 measurement obtained in the outpatient clinic was 58 mm Hg. Supplemental oxygen at night was reduced. Excessive oxygen supplementation may result in CO_2 retention. Oxygen should be titrated to maintain SpO_2 not higher than 92% at rest.

EPAP was decreased to 8 cm H_2O and Ti range to 0.8 to 1.1 s, but an attempt at increasing IPAP was not tolerated. Overnight transcutaneous CO_2 showed a mean of 54 mm Hg, fluctuating depending on leak (incompletely controlled). Because of increasing daytime NIV use, mouthpiece ventilation was added to help with dyspnea during daily activities. It allowed the patient to perform some work in his garage, for which he was grateful. About 24 months after starting NIV, he remained at home with no further hospitalizations, despite exacerbations requiring antibiotic and corticosteroid treatment. Despite imperfect CO_2 control, the patient was stabilized and rehospitalizations to date have been averted.

Approach to Home NIV in COPD

Initiation Setting

No optimal initiation location has been agreed on. The ATS suggests against titrating NIV in the sleep laboratory because of concerns regarding cost, delay, safety of achieving rapid normocapnia over a single night, and proficiency of personnel in such titrations.[33] European studies used initiation in hospital, often in specialized ventilation units, over days, with progressive acclimatization and optimization.[5,17,25] This is not possible currently in most North American centers. However, parameters used and tolerated during an acute exacerbation can be a useful starting point. Titration performed while admitted for an acute exacerbation is practical, but chronic hypercapnia should be confirmed before starting LTNIV, and parameters should be reassessed based on ventilation goals.

Home initiation has been studied as an alternative to in-hospital initiation.[35] The protocol required multiple home visits and daily calls from a specialized nurse and remote monitoring of ventilator and overnight transcutaneous CO_2 data, and lasted a median of 7 days. Technical difficulties affected transcutaneous CO_2 measurements in a significant proportion of patients. This protocol was shown to be noninferior to hospital initiation, cheaper, and safe (patients with unstable cardiac comorbidities or heart failure were excluded). This highly resource-intensive protocol is promising, but likely would require further optimization and adaptation to local realities.

In our experience, NIV initiation often takes place in the outpatient setting, using a combination of resources, ideally specialized respiratory therapists, available in clinic and at home. Clinic visits may include discussions regarding NIV potential benefits and challenges with shared decision-making regarding initiation, training on equipment, and interface selection. A daytime NIV trial may be performed, starting at low pressures and increasing pressures as tolerated during quiet wakefulness. Alternatively, initiation may be performed directly at home using trained home care or medical equipment providers.

Close follow-up in the initial period after starting NIV is important. Trained staff (ideally a respiratory therapist) should follow up within days to provide support and optimize interface and ventilation comfort. This could be done remotely, including for parameter adjustments (for non-life support devices),[35] provided that adequate connectivity is available. New mask trials, if needed, should be carried out in person. The extent to which this is performed by home care or equipment companies vs clinic staff may vary based on local resources. Physician follow-up should occur within weeks to assess adherence, comfort, and partial pressure of carbon dioxide (P_{CO_2}) (arterial, capillary, or transcutaneous CO_2) to inform further parameter adjustments. We suggest targeting reduction of daytime P_{CO_2} by $\geq$ 20%, or to $<$ 48 mm Hg if possible.[5] Adjustments then can be completed targeting nocturnal gas exchange[25] based on overnight transcutaneous CO_2 or oximetry, remembering that the latter will not be reliable regarding hypoventilation in patients receiving LTOT. With this type of outpatient protocol, reaching optimal parameters may take longer than with hospital-based initiation, but an outpatient protocol may constitute a lesser burden on patients and health care resources.

Mask Choice

The choice of mask (Table 1) is crucial for initiation and adaptation to LTNIV and is a key issue for most individuals who use NIV and caregivers.[36] Oronasal interfaces seem to be used most frequently,[36] possibly because of oronasal mask use during hospitalizations. Additionally, patients with more extreme dyspnea may be unable to breathe exclusively through the nose, precluding use of a nasal interface. However, nasal masks still should be considered because they cover a smaller facial area, and hence are less prone to leaks and might be easier to apply. A chin strap can help counter mouth leak[37] for patients able to use one. Nasal masks also have less potential for exacerbating upper airway obstruction,[38,39] but this has not been studied in the context of NIV.

TABLE 1] Principles of Mask Selection and Application

Always confirm mask fit with NIV on
Lift the mask to inflate the air cushion, before tightening the headgears
Use the minimum tension required on the headgear
Always try the mask in the position it will be used
Verify that the patient can apply the mask correctly and without excessive effort
Clean the mask daily to remove the film left by skin sebum

NIV = noninvasive ventilation.

To improve adherence, the chosen mask must be comfortable and easy to handle. Patients applying their mask independently must be able to do it easily and quickly if dyspneic. If experiencing difficulty lifting the arms up to the head, strategies should be developed to limit required movement during mask application. A well-fitting mask can determine adherence by minimizing uncomfortable pressure points and preventing leaks, which can be bothersome, can cause asynchrony, can reduce effectiveness of ventilation, and can introduce errors into reported ventilation.

NIV Parameters

Pressures: Achieving significant P_{CO_2} reduction is the main goal of NIV, along with resting of the diaphragm and accessory muscles. Using bilevel NIV, this typically requires high driving pressures (IPAP, $>$ 18 cm H_2O) to overcome high airways resistance that also is present in inspiration in severe COPD. This results in larger tidal volumes, allowing adequate alveolar ventilation in the context of increased dead space and lower respiratory rates to help reduce hyperinflation.[22] In an NIV treatment-naive patient, IPAP can be started at 12 cm H_2O and increased empirically to the maximum tolerated, aiming for a normalizing P_{CO_2}.[22] Pressures of up to 42 cm H_2O have been reported,[40] although values of $>$ 30 cm H_2O are unusual. Although IPAP may need to be increased gradually to allow patient adaptation, it has been shown that adherence is better with higher compared with lower pressures, in addition to improved P_{CO_2}, dyspnea, and FEV_1.[21]

Volume-assured pressure support methods (average volume-assured pressure support or intelligent volume-assured pressure support), with or without auto-EPAP,

can be a good option for autotitration or for long-term use. However, mask leaks must be controlled for device algorithms to function properly. They seem to be equivalent with respect to efficacy to fixed pressure support modes,[41,42] although some evidence suggests that auto-EPAP can be superior regarding P_{CO_2} control and symptoms.[43,44] A starting target tidal volume of 6 to 8 mL/kg of ideal body weight can be used, with subsequent adjustment to optimize P_{CO_2} and comfort. The set minimal IPAP should be sufficiently high to ensure that the target volume is reached through support provided primarily by the device, rather than a patient-generated effort.

The EPAP traditionally has been set at low values in patients with COPD without obesity. A level of 3 to 5 cm H_2O should be used to start (devices limit minimum EPAP to 3-4 cm H_2O to prevent rebreathing in a single-limb passive circuit). However, higher EPAP may be needed to correct upper airway obstruction[45] and can be titrated during polysomnography or using an auto-EPAP mode. EPAP also can help match intrinsic positive end-expiratory pressure, reducing triggering effort and asynchrony.[46] However, intrinsic positive end-expiratory pressure cannot be measured easily. Some evidence suggests that higher EPAP also may correct expiratory flow limitation by stenting the airways during expiration,[46] which could improve comfort and reduce hyperinflation. NIV devices with self-adjusting EPAP targeting expiratory flow limitation exist, but are not widely available and require further study. Manual adjustment optimizing patient device triggering and comfort remains necessary.

Backup Rate and Trigger Sensitivity: Effective triggering is important for optimal synchrony to minimize work of breathing and for comfort.[12] In addition to optimizing mask fit and EPAP, this can be achieved by adjusting trigger sensitivity in many devices, starting with medium. Initial high-intensity protocols included high BUR to control ventilation and to minimize patient effort.[47] However, it has been shown that with adequate pressures, a high BUR does not provide further benefit or unloading of respiratory muscles.[23] In the United States, obtaining a device for COPD with a BUR often requires either prescribing a ventilator or a spontaneous bilevel device failing. For patients with less severe disease, starting without a BUR may be reasonable. For patients with more severe disease, obtaining a device with a BUR is advisable. When using a BUR, we suggest starting at 12/min and titrating up only after optimizing pressures, triggering, and Ti cycling. Overly aggressive

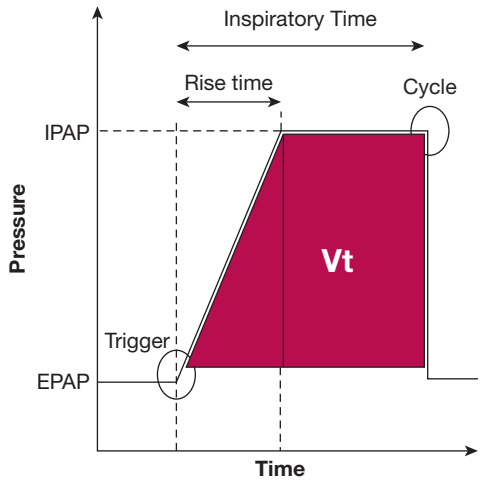

Figure 1 – *Diagram showing the main elements of a bilevel noninvasive ventilation device-supported breath. EPAP = expiratory positive airway pressure; IPAP = inspiratory positive airway pressure; Vt = tidal volume. (Reprinted with permission from Selim et al.[49])*

BUR may exacerbate patient-ventilator asynchrony (eg, glottic closure)[48] and may promote intolerance.

Ti and Cycling Off: Longer expiratory time helps to reduce hyperinflation in COPD; hence, a shorter Ti (Fig 1)[49] is beneficial, provided that ventilation remains adequate. Delayed cycling off (returning from IPAP to EPAP) can lead to asynchrony during flow-based cycling modes like bilevel spontaneous (S) or spontaneous timed (ST) and volume-assured pressure support (VAPS) (Fig 2).[50] Cycling off therefore should be set at high sensitivity (earlier). Uncontrolled leaks may prevent synchronized cycling. Pressure (assist) control modes,

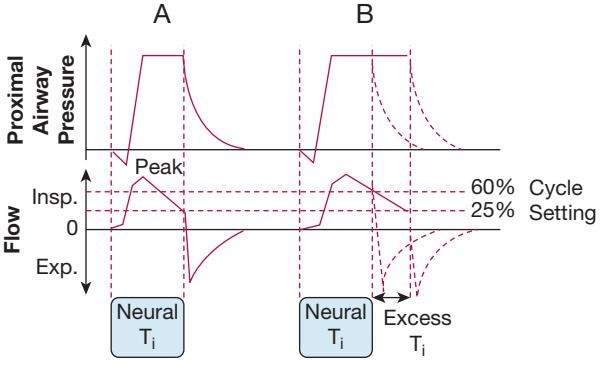

Figure 2 – *Diagram showing how cycling threshold affects the duration of respiration. A, Normal respiratory mechanics. The cycle setting is 25% of peak inspiratory flow. Cycling is ideal, as indicated by the fact that the inspiratory flow decreases to the 25% cycling level at the end of the patient's neural Ti. B, Obstructive respiratory mechanics. The change in the inspiratory flow curve leads to the 25% level being reached later, well after the end of the neural Ti. The duration of delayed cycling is represented by the excess Ti. Increasing the cycle setting to 60% of peak inspiratory flow corrects this problem, and cycling occurs at the end of neural Ti. Exp = expiration; Insp = inspiration; Ti = inspiratory time. (Reprinted with permission from Jolliet.[50])*

where the Ti is fixed for all breaths, can be useful to remedy these problems. For bilevel S or spontaneous-timed and some volume-assured pressure support modes, many devices allow limits on Ti on spontaneous breaths (minimum or maximum Ti); device-triggered breaths have a fixed Ti. We suggest a Ti minimum and maximum starting range of 0.5 to 1.0 s.

Rise Time: Patients with COPD often have so-called air hunger. A rapid pressure rise from EPAP to IPAP provides high flow when inspiration is triggered, reducing the work of breathing.[51] This also allows target IPAP to be reached faster and a higher volume to be delivered for a given Ti.

Ramp Up and Ramp Down: Bilevel devices may have a ramp-up feature allowing pressures to increase progressively when started. This can help when high IPAP is difficult to tolerate. Yet if pressures are too low, this may be uncomfortable and may result in uncontrolled hypoventilation[52]; hence, this should be applied judiciously and followed up.

Some patients with COPD experience prolonged dyspnea on stopping NIV in the morning, termed *deventilation syndrome*.[53] It can be remedied by adjusting parameters and improving synchrony.[53] Some devices now also include a ramp-down feature where pressures decrease gradually for an intended smoother transition to spontaneous breathing, but no clinical data are available on this feature.

Comorbidities

A significant proportion of patients with COPD also have OSA, obesity, or another restrictive condition such as kyphoscoliosis. OSA can be corrected by adapting EPAP. However, the literature is scant on how to approach other parameters in the context of mixed obstructive and restrictive syndromes. Although NIV for restrictive conditions also requires high IPAP, one typically would use longer Ti, slower rise time, and delayed cycling off. Our practice typically is dictated by the primary spirometric abnormality. In a patient with milder COPD with a primarily restrictive syndrome, we chose parameters targeting the restriction. Adjustments are made as needed to optimize comfort, synchrony, and gas exchange.

Monitoring

Monitoring of symptoms and daytime P_{CO_2} are key elements providing the clinician with feedback regarding NIV effectiveness. Overnight gas exchange should be assessed.[54] Oximetry is used frequently, but is difficult to interpret with supplemental oxygen. Overnight home transcutaneous CO_2 is useful,[55] but remains technically challenging, expensive, and not widely available in North America. Device recordings (either via manual download or cloud-based remote monitoring) can help to ascertain adherence, interface adjustment (leak), and more detailed ventilation outcomes.[56] Importantly, download data, such as tidal volume and minute ventilation, are inaccurate in the face of significant leak.

Applications Beyond Nighttime Use

Patients with more extreme dyspnea may benefit from NIV extension into the daytime. This can be achieved using the same settings as for sleep, eg, during a rest period, but favoring a nasal mask to allow easier speech. Open circuit mouthpiece ventilation[57] allows more freedom and mobility and improves the ability to communicate. Commercial home ventilators now have dedicated mouthpiece ventilation modes and circuits. Handheld portable devices have been shown to improve dyspnea and walking distance,[58] but can be heavy and impractical.

Conclusions

Data are accumulating suggesting that home LTNIV in patients with hypercapnic severe COPD can improve clinical and patient-related outcomes when the parameters are adapted to COPD physiologic characteristics. Many questions remain regarding patient selection and implementation. Patients with COPD bring a different set of challenges compared with other populations requiring home NIV. Pulmonologists inevitably will be faced with increasing demand that will require locally adapted protocols and care pathways to optimize delivery of this therapy.

Financial/Nonfinancial Disclosures

The authors have reported to *CHEST* the following: M. K. reports research grants from CHEST and Canadian Institutes of Health Research, investigator-initiated research support from Philips, and advisory board membership for Biron Soins du Sommeil. J. E. O. receives research funding from the National Heart, Lung, and Blood Institute, National Institutes of Health. J. E. O. participates in an advisory board for Resmed, Inc. None declared (V. A.).

Acknowledgment

Other contributions: The authors thank the staff of the Quebec National Program for Home Ventilatory Assistance, McGill University

Health Center, for their dedication to their patients and the excellence of their work.

References

1. World Health Organization. The top 10 causes of death. 2020. World Health Organization website. Accessed November 15, 2023. https://www.who.int/news-room/fact-sheets/detail/the-top-10-causes-of-death
2. Casanova C, Celli BR, Tost L, et al. Long-term controlled trial of nocturnal nasal positive pressure ventilation in patients with severe COPD. *Chest*. 2000;118(6):1582-1590.
3. Clini E, Sturani C, Rossi A, et al. The Italian multicentre study on noninvasive ventilation in chronic obstructive pulmonary disease patients. *Eur Respir J*. 2002;20(3):529-538.
4. McEvoy RD, Pierce RJ, Hillman D, et al. Nocturnal non-invasive nasal ventilation in stable hypercapnic COPD: a randomised controlled trial. *Thorax*. 2009;64(7):561-566.
5. Kohnlein T, Windisch W, Kohler D, et al. Non-invasive positive pressure ventilation for the treatment of severe stable chronic obstructive pulmonary disease: a prospective, multicentre, randomised, controlled clinical trial. *Lancet Respir Med*. 2014;2(9):698-705.
6. Connors AF Jr, Dawson NV, Thomas C, et al. Outcomes following acute exacerbation of severe chronic obstructive lung disease. The SUPPORT investigators (Study to Understand Prognoses and Preferences for Outcomes and Risks of Treatments). *Am J Respir Crit Care Med*. 1996;154(4 pt 1):959-967.
7. Rochwerg B, Brochard L, Elliott MW, et al. Official ERS/ATS clinical practice guidelines: noninvasive ventilation for acute respiratory failure. *Eur Respir J*. 2017;50(2):1602426.
8. Chandra D, Stamm JA, Taylor B, et al. Outcomes of noninvasive ventilation for acute exacerbations of chronic obstructive pulmonary disease in the United States, 1998-2008. *Am J Respir Crit Care Med*. 2012;185(2):152-159.
9. Elliott MW, Nava S. Noninvasive ventilation for acute exacerbations of chronic obstructive pulmonary disease: "Don't think twice, it's alright!.". *Am J Respir Crit Care Med*. 2012;185(2):121-123.
10. Lindenauer PK, Stefan MS, Shieh MS, Pekow PS, Rothberg MB, Hill NS. Outcomes associated with invasive and noninvasive ventilation among patients hospitalized with exacerbations of chronic obstructive pulmonary disease. *JAMA Intern Med*. 2014;174(12):1982-1993.
11. Struik FM, Lacasse Y, Goldstein RS, Kerstjens HA, Wijkstra PJ. Nocturnal noninvasive positive pressure ventilation in stable COPD: a systematic review and individual patient data meta-analysis. *Respir Med*. 2014;108(2):329-337.
12. Lloyd-Owen SJ, Donaldson GC, Ambrosino N, et al. Patterns of home mechanical ventilation use in Europe: results from the Eurovent survey. *Eur Respir J*. 2005;25(6):1025-1031.
13. Cantero C, Adler D, Pasquina P, et al. Long-term noninvasive ventilation in the Geneva Lake area: indications, prevalence, and modalities. *Chest*. 2020;158(1):279-291.
14. Patout M, Lhuillier E, Kaltsakas G, et al. Long-term survival following initiation of home non-invasive ventilation: a European study. *Thorax*. 2020;75(11):965-973.
15. Rose L, McKim DA, Katz SL, et al. Home mechanical ventilation in Canada: a national survey. *Respir Care*. 2015;60(5):695-704.
16. Frazier WD, DaVanzo JE, Dobson A, Heath S, Mati K. Early initiation of non-invasive ventilation at home improves survival and reduces healthcare costs in COPD patients with chronic hypercapnic respiratory failure: a retrospective cohort study. *Respir Med*. 2022;200:106920.
17. van der Leest S, Duiverman ML. High-intensity non-invasive ventilation in stable hypercapnic COPD: evidence of efficacy and practical advice. *Respirology*. 2019;24(4):318-328.
18. Struik FM, Lacasse Y, Goldstein R, Kerstjens HM, Wijkstra PJ. Nocturnal non-invasive positive pressure ventilation for stable chronic obstructive pulmonary disease. *Cochrane Database Syst Rev*. 2013;(6):CD002878.
19. Elliott MW. Domiciliary non-invasive ventilation in stable COPD? *Thorax*. 2009;64(7):553-556.
20. Schwarz SB, Magnet FS, Windisch W. Why high-intensity NPPV is favourable to low-intensity NPPV: clinical and physiological reasons. *COPD*. 2017;14(4):389-395.
21. Dreher M, Storre JH, Schmoor C, Windisch W. High-intensity versus low-intensity non-invasive ventilation in patients with stable hypercapnic COPD: a randomised crossover trial. *Thorax*. 2010;65(4):303-308.
22. Díaz O, Bégin P, Torrealba B, Jover E, Lisboa C. Effects of noninvasive ventilation on lung hyperinflation in stable hypercapnic COPD. *Eur Respir J*. 2002;20(6):1490-1498.
23. Murphy PB, Brignall K, Moxham J, Polkey MI, Davidson AC, Hart N. High pressure versus high intensity noninvasive ventilation in stable hypercapnic chronic obstructive pulmonary disease: a randomized crossover trial. *Int J Chron Obstruct Pulmon Dis*. 2012;7:811-818.
24. Duiverman ML, Huberts AS, van Eykern LA, Bladder G, Wijkstra PJ. Respiratory muscle activity and patient-ventilator asynchrony during different settings of noninvasive ventilation in stable hypercapnic COPD: does high inspiratory pressure lead to respiratory muscle unloading? *Int J Chron Obstruct Pulmon Dis*. 2017;12:243-257.
25. 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: a randomized clinical trial. *JAMA*. 2017;317(21):2177-2186.
26. Struik FM, Sprooten RT, Kerstjens HA, et al. Nocturnal non-invasive ventilation in COPD patients with prolonged hypercapnia after ventilatory support for acute respiratory failure: a randomised, controlled, parallel-group study. *Thorax*. 2014;69(9):826-834.
27. Cherian M, Adam V, Ross B, Bourbeau J, Kaminska M. Mortality in individuals with COPD on long-term home non-invasive ventilation. *Respir Med*. 2023;218:107378.
28. Galli JA, Krahnke JS, James Mamary A, Shenoy K, Zhao H, Criner GJ. Home non-invasive ventilation use following acute hypercapnic respiratory failure in COPD. *Respir Med*. 2014;108(5):722-728.
29. Coughlin S, Liang WE, Parthasarathy S. Retrospective assessment of home ventilation to reduce rehospitalization in chronic obstructive pulmonary disease. *J Clin Sleep Med*. 2015;11(6):663-670.
30. Frazier WD, Murphy R, van Eijndhoven E. Non-invasive ventilation at home improves survival and decreases healthcare utilization in medicare beneficiaries with chronic obstructive pulmonary disease with chronic respiratory failure. *Respir Med*. 2020;177:106291.
31. Frazier W, van Eijndhoven E, Murphy R, Jena AB. Noninvasive ventilation at home reduces mortality in COPD with CRF. *Am J Manag Care*. 2021;27(9):e308-e315.
32. Ergan B, Oczkowski S, Rochwerg B, et al. European Respiratory Society guidelines on long-term home non-invasive ventilation for management of COPD. *Eur Respir J*. 2019;54(3):1901003.
33. Macrea M, Oczkowski S, Rochwerg B, et al. Long-term noninvasive ventilation in chronic stable hypercapnic chronic obstructive pulmonary disease. An official American Thoracic Society clinical practice guideline. *Am J Respir Crit Care Med*. 2020;202(4):e74-e87.
34. Kaminska M, Rimmer KP, Nonoyama M, et al. Long-term non-invasive ventilation in patients with chronic obstructive pulmonary disease (COPD): 2021 Canadian Thoracic Society clinical practice guideline update. *Can J Respir Crit Care Sleep Med*. 2021;5(3):160-183.
35. Duiverman ML, Vonk JM, Bladder G, et al. Home initiation of chronic non-invasive ventilation in COPD patients with chronic hypercapnic respiratory failure: a randomised controlled trial. *Thorax*. 2020;75(3):244-252.
36. Masefield S, Vitacca M, Dreher M, et al. Attitudes and preferences of home mechanical ventilation users from four European countries: an ERS/ELF survey. *ERJ Open Res*. 2017;3(2):00015-02017.
37. Gonzalez J, Sharshar T, Hart N, Chadda K, Raphaël JC, Lofaso F. Air leaks during mechanical ventilation as a cause of persistent hypercapnia in neuromuscular disorders. *Intensive Care Med*. 2003;29(4):596-602.

38. Genta PR, Kaminska M, Edwards BA, et al. The importance of mask selection on continuous positive airway pressure outcomes for obstructive sleep apnea. An official American Thoracic Society workshop report. *Ann Am Thorac Soc*. 2020;17(10):1177-1185.

39. Kaminska M, Montpetit A, Mathieu A, Jobin V, Morisson F, Mayer P. Higher effective oronasal versus nasal continuous positive airway pressure in obstructive sleep apnea: effect of mandibular stabilization. *Can Respir J*. 2014;21(4):234-238.

40. Windisch W, Haenel M, Storre JH, Dreher M. High-intensity non-invasive positive pressure ventilation for stable hypercapnic COPD. *Int J Med Sci*. 2009;6(2):72-76.

41. Orr JE, Coleman J, Criner GJ, et al. Automatic EPAP intelligent volume-assured pressure support is effective in patients with chronic respiratory failure: a randomized trial. *Respirology*. 2019;24(12):1204-1211.

42. Crisafulli E, Manni G, Kidonias M, Trianni L, Clini EM. Subjective sleep quality during average volume assured pressure support (AVAPS) ventilation in patients with hypercapnic COPD: a physiological pilot study. *Lung*. 2009;187(5):299-305.

43. Magdy DM, Metwally A. Auto-titrating versus fixed-EPAP intelligent volume-assured pressure support (iVAPS) ventilation in patients with COPD and hypercapnic respiratory failure. *Adv Respir Med*. 2021;89(3):277-283.

44. Gursel G, Zerman A, Basarik B, Gonderen K, Aydogdu M, Memmedova S. Noninvasive auto-titrating ventilation (AVAPS-AE) versus average volume-assured pressure support (AVAPS) ventilation in hypercapnic respiratory failure patients. *Intern Emerg Med*. 2018;13(3):359-365.

45. Czerwaty K, Dżaman K, Sobczyk KM, Sikorska KI. The overlap syndrome of obstructive sleep apnea and chronic obstructive pulmonary disease: a systematic review. *Biomedicines*. 2022;11(1):16.

46. Zannin E, Milesi I, Porta R, et al. Effect of nocturnal EPAP titration to abolish tidal expiratory flow limitation in COPD patients with chronic hypercapnia: a randomized, cross-over pilot study. *Respir Res*. 2020;21(1):301.

47. Windisch W, Vogel M, Sorichter S, et al. Normocapnia during nIPPV in chronic hypercapnic COPD reduces subsequent spontaneous $PaCO_2$. *Respir Med*. 2002;96(8):572-579.

48. Aboussouan LS, Mireles-Cabodevila E. Sleep-disordered breathing in neuromuscular disease: diagnostic and therapeutic challenges. *Chest*. 2017;152(4):880-892.

49. Selim BJ, Wolfe L, Coleman JM 3rd, Dewan NA. Initiation of noninvasive ventilation for sleep related hypoventilation disorders: advanced modes and devices. *Chest*. 2018;153:251-265.

50. Jolliet P. Clinical review: patient-ventilator interaction in chronic obstructive pulmonary disease. *Crit Care*. 2006;10(6):236.

51. Murata S, Yokoyama K, Sakamoto Y, et al. Effects of inspiratory rise time on triggering work load during pressure-support ventilation: a lung model study. *Respir Care*. 2010;55(7):878-884.

52. Gonzalez-Bermejo J, Rabec C, Perrin C, et al. Treatment failure due to use of a 'ramp' option on pressure support home ventilators. *Thorax*. 2016;71(8):764-766.

53. Adler D, Perrig S, Takahashi H, et al. Polysomnography in stable COPD under non-invasive ventilation to reduce patient-ventilator asynchrony and morning breathlessness. *Sleep Breath*. 2012;16(4):1081-1090.

54. Arnal J-M, Oranger M, Gonzalez-Bermejo J. Monitoring systems in home ventilation. *J Clin Med*. 2023;12(6):2163.

55. Georges M, Rabec C, Monin E, et al. Monitoring of noninvasive ventilation: comparative analysis of different strategies. *Respir Res*. 2020;21(1):324.

56. Choi P, Adam V, Zielinski D. Noninvasive ventilation downloads and monitoring. *Sleep Med Clin*. 2020;15(4):569-579.

57. Toussaint M, Chatwin M, Gonçalves MR, et al. Mouthpiece ventilation in neuromuscular disorders: narrative review of technical issues important for clinical success. *Respir Med*. 2021;180:106373.

58. Majorski DS, Magnet FS, Thilemann S, Schmoor C, Windisch W, Schwarz SB. Portable NIV for patients with moderate to severe COPD: two randomized crossover trials. *Respir Res*. 2021;22(1):123.