

What matters to people with COPD: outputs from Working Together for Change (2019)

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Chronic obstructive pulmonary disease (COPD) is a progressive lung disease and a significant cause of morbidity and mortality around the globe.^{1,2} COPD impacts negatively on quality of life, with breathlessness affecting everyday activities including dressing, washing and eating.³⁻⁵ Breathlessness is a subjective experience and functional performance can vary among people with the same degree of airflow obstruction.⁶ Spontaneous activity levels may be reduced, particularly as the condition progresses^{7,8} and patients may spend less time engaged in personal care and chores and have lower median sleep duration.⁹ There are further detrimental impacts of social isolation, loneliness, embarrassment, loss of independence and fatigue.¹⁰ More so than other chronic conditions, COPD causes biographical disruption due to time spent managing health and activities of daily living.^{11,12} Affecting mental and emotional well-being, COPD becomes a way of life for many people with severe disease.¹³

Engagement and participation in a variety of activities enhances well-being and is a legitimate focus for interventions to support people in managing their lives with COPD. It is important to people with COPD to maintain social interactions and a sense of normality, freedom and purpose.⁵ ***Health services, however, are often based on the medical model and may not address social and emotional aspects of patients' lives. What matters most to patients and to clinicians may not be the same.***

REFERENCE: Early F, Lettis M, Winders SJ, Fuld J. What matters to people with COPD: outputs from Working Together for Change. *NPJ Prim Care Respir Med.* 2019;29(1):11.

INTRODUCTION:

In patients with chronic hypercapnic respiratory failure, long-term non-invasive positive pressure ventilation (NPPV) has been shown to improve important physiological variables such as blood gases and lung hyperinflation.⁵ Results from clinical studies showed improvements in exercise capacity (6-min walk distance,⁶ exercise-related dyspnoea,⁷ pulmonary cachexia,⁸ and sleep quality⁹). Furthermore, disease-specific aspects of health-related quality of life (HRQL) reportedly improve in patients with COPD following long-term NPPV.¹⁰

While the efficacy of home non-invasive ventilation (NIV) has been well proven, there still remains some controversy over its application. COPD patients with chronic hypercapnic respiratory failure are increasingly treated with long-term noninvasive ventilation (NIV) at home due to its association with improved survival rates, better health-related quality of life (HRQL) and increased exercise capacity after treatment commencement.¹⁻³ It has been shown that stable COPD patients are markedly inactive in their daily lives, with the majority of the day spent sitting or lying down.⁴ Focus should also be placed on portable NIV devices to support daily physical activities as a component of COPD disease management.

Recent studies have been included for this review with evidence that continues to show outcomes supporting long term home NIV use is safe for management of stable COPD patients with chronic respiratory failure (CRF).

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2. 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.
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4. Pitta F, Troosters T, Spruit MA, et al. Characteristics of physical activities in daily life in chronic obstructive pulmonary disease. *Am J Respir Crit Care Med* 2005; 171:972–977.
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6. Funk GC, Breyer MK, Burghuber OC, et al. Long-term non-invasive ventilation in COPD after acute-on-chronic respiratory failure. *Respir Med* 2011; **105**: 427–34.
7. Tsolaki V, Pastaka C, Karetsi E, et al. One-year non-invasive ventilation in chronic hypercapnic COPD: effect on quality of life. *Respir Med* 2008; **102**: 904–11.
8. Budweiser S, Heinemann F, Meyer K, Wild PJ, Pfeifer M. Weight gain in cachectic COPD patients receiving noninvasive positive-pressure ventilation. *Respir Care* 2006; **51**: 126–32.
9. Meecham Jones DJ, Paul EA, Jones PW, Wedzicha JA. Nasal pressure support ventilation plus oxygen compared with oxygen therapy alone in hypercapnic COPD. *Am J Respir Crit Care Med* 1995; **152**: 538–44.
10. Windisch W, Quality of life in home mechanical ventilation study group. Impact of home mechanical ventilation on health-related quality of life. *Eur Respir J* 2008; **32**: 1328–36.

ASSESSMENT OF OUTCOMES

DECREASED MORTALITY:

1. Physical Activity Is the Strongest Predictor of All-Cause Mortality in Patients With COPD A Prospective Cohort Study (2011)

METHODS: In a prospective cohort study of 170 outpatients with stable COPD (mean FEV₁, 56% predicted), we assessed lung function by spirometry and body plethysmography; physical activity level (PAL) by a multisensory armband; exercise capacity by 6-min walk distance test; cardiovascular status by echocardiography, vascular Doppler sonography (ankle-brachial index [ABI]), and N-terminal pro-B-type natriuretic peptide level; nutritional and muscular status by BMI and fat-free mass index; biomarkers by levels of high-sensitivity C-reactive protein, IL-6, fibronectin, adiponectin, and leptin; and health status, dyspnea, and depressive symptoms by questionnaire. Established prognostic indices were calculated. The median follow-up was 48 months (range, 10-53 months).

RESULTS: All-cause mortality was 15.4%. After adjustments, each 0.14 increase in PAL was associated with a lower risk of death (hazard ratio [HR], 0.46; 95% CI, 0.33-0.64; P 0.001). Compared with established predictors, PAL showed the best discriminative properties for 4-year survival (C statistic, 0.81) and was associated with the highest relative risk of death per standardized decrease. Novel predictors of mortality were adiponectin level (HR, 1.34; 95% CI, 1.06-1.71; P 5 .017), leptin level (HR, 0.81; 95% CI, 0.65-0.99; P 5 .042), right ventricular function (Tei-index) (HR, 1.26; 95% CI, 1.04-1.54; P 5 .020), and ABI, 1.00 (HR, 3.87; 95% CI, 1.44-10.40; P 5 .007). A stepwise Cox regression revealed that the best model of independent predictors was PAL, adiponectin level, and ABI. The composite of these factors further improved the discriminative properties (C statistic, 0.85).

CONCLUSIONS: We found that objectively measured physical activity is the strongest predictor of all-cause mortality in patients with COPD. In addition, adiponectin level and vascular status provide independent prognostic information in our cohort.

DISCUSSION: *Strong evidence to show the importance of physical activity and further supporting the evidence for home NIV and/or pNIV devices in this patient population.*

REFERENCE: Waschki B, Kirsten A, Holz O, Muller KC, Meyer T, Watz H, et al. Physical activity is the strongest predictor of all-cause mortality in patients with COPD: a prospective cohort study. *Chest* 2011; 140(2): 331-342.

2. Non-invasive positive pressure ventilation for the treatment of severe stable chronic obstructive pulmonary disease: a prospective, multicentre, randomised, controlled clinical trial (2014)

METHOD: This investigator-initiated, prospective, multicentre, randomised, controlled clinical trial enrolled patients with stable GOLD stage IV COPD and a partial carbon dioxide pressure (PaCO₂) of 51.9 mm Hg or higher and pH higher than 7.35. NPPV was targeted to reduce baseline PaCO₂ by at least 20% or to achieve PaCO₂ values lower than 48.1 mmHg. Patients were randomly assigned (in a 1:1 ratio) via a computer-generated randomisation sequence with a block size of four, to continue optimised standard treatment (control group) or to receive additional NPPV for at least 12 months (intervention group). The primary outcome was 1-year all-cause mortality. Analysis was by intention to treat. The intervention was unblinded, but outcome assessment was blinded to treatment assignment.

RESULTS: 195 patients were randomly assigned to the NPPV group (n=102) or to the control group (n=93). All patients from the control group and the NPPV group were included in the primary analysis. 1-year mortality was 12% (12 of 102 patients) in the intervention group and 33% (31 of 93 patients) in the control group; hazard ratio 0.24 (95% CI 0.11–0.49; p=0.0004). 14 (14%) patients reported facial skin rash, which could be managed by changing the type of the mask. No other intervention-related adverse events were reported.

CONCLUSION: The addition of long-term NPPV to standard treatment improves survival of patients with hypercapnic, stable COPD when NPPV is targeted to greatly reduce hypercapnia.

COMMENTS: *Strong evidence, good sample size. Criteria to lower PaCO₂ by 20% or 48.1mmHg would require lab testing or tCO₂ monitoring.*

REFERENCE: Köhnlein T, Windisch W, Köhler 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;2:698–705

DECREASED HOSPITAL ADMISSIONS SECONDARY TO EXACERBATIONS and/or HOSPITAL RE-ADMISSIONS FOR RESPIRATORY RELATED DISEASE

1. Health Care Utilization and Respiratory Status Following the Addition of a Portable Non-Invasive Open Ventilator (NIOV) to the Treatment Regimen (2015)

METHOD: Retrospective analysis of 16 stable oxygen-dependent patients with moderate to severe chronic lung disease. The following data was collected and reviewed:

- Diagnosis, demographic/clinical characteristics

- Respiratory function
- Physician visits, ER visits, hospital and ICU admissions
- Inpatient and ICU days, mechanical ventilation days
- 2 patient-reported measures of respiratory status (CAT and mMRC)

RESULTS: In this group of ambulatory patients with chronic respiratory insufficiency, introduction of the NIOV System was associated with:

- Statistically significant decrease in health care utilization across four of five health care utilization measures: emergency room visits, hospital days, hospital ICU days and mechanical ventilations.
- Estimated total cost reductions across the study population of between 68 and 96 percent. Office visits were the only measure that did not achieve significant decreases in frequency or cost.
- *COPD Assessment Test (CAT) and modified Medical Research Council (mMRC) scores improved significantly in the post-NIOV implementation period ($p < 0.0001$ and $p = 0.0001$, respectively).*

CONCLUSION: In this group of ambulatory patients with chronic respiratory insufficiency, introduction of the NIOV System was associated with significantly decreased utilization of inpatient health care services and improved self-reported respiratory status.

COMMENTS: *Small sample size but results statistically significant. Office visits are an important part of disease management and patient follow up.*

REFERENCE: MacIntyre, N. et al; CHEST, OCT 2015; Vol 148:4; 908A.

INCREASED PHYSICAL FUNCTION and/or QUALITY OF LIFE:

1. Intermittent Use of Portable NIV Increases Exercise Tolerance in COPD: A Randomised, Cross Over Trial. (2019)

METHOD: This was a randomised, open-label cross-over trial comparing the use of pNIV to PLB during recovery periods in two different intermittent exercise regimes (Figure 1). Patients underwent a ramp incremental cardiopulmonary exercise test (CPET) to determine WRpeak, and then were randomly assigned to a high-intensity (HI) or a moderate-intensity (MOD) protocol. Within these groups, each patient performed two more visits using both pNIV and PLB during recovery from exercise in balanced order (see below); the primary outcome was exercise endurance time (TLim). Patients were on optimal bronchodilator therapy including daily LAMA and LABA and no changes to medication were made during the trial. Tests were performed without supplemental oxygen. Following the last visit, all 24 patients were given a VitaBreath device to use it as they wished and were contacted at 2 and 12 weeks to assess their use of, and attitudes towards, the device. Patients received advice on the use of the device for symptomatic relief after exertion, but the frequency of use was not prescribed.

RESULTS: This study showed that the use of pNIV (VitaBreath) during intermittent exercise is associated with longer exercise endurance time (by 19–20%), with less dynamic hyperinflation and breathlessness when compared to purse lip breathing. Compared to PLB, pNIV increased exercise tolerance (HI: by 5.2 ± 6.0 min; MOD: by 5.8 ± 6.7 min) ($p < 0.05$). With pNIV, mean inspiratory capacity increased and breathlessness decreased by clinically meaningful margins during recovery compared to the end of exercise (HI: by 140 ± 110 mL and 1.2 ± 1.7 ; MOD: by 170 ± 80 mL and 1.0 ± 0.7). At 12 weeks, patients reported that pNIV reduced anxiety (median: 7.5/10 versus 4/10, $p = 0.001$) and recovery time

from breathlessness (17/24 patients; $p = 0.002$); 23/24 used the device at least weekly. pNIV increased exercise tolerance by reducing dynamic hyperinflation and breathlessness in COPD patients.

CONCLUSION: The major finding of the study is that the use of pNIV during recovery periods interspersing moderate- and high-intensity bouts of intermittent exercise significantly improved exercise tolerance compared to PLB. This is probably due to more rapid recovery from exercise-induced dynamic hyperinflation, with associated improvements in cardiac output and systemic oxygen delivery. The physiological responses shown were matched by a reduction in breathlessness and leg discomfort in recovery from exercise. Patients reported that the VitaBreath device improved anxiety around breathlessness, as well as perceived time of recovery from it during activities of daily living.

COMMENTS: *Small sample size. VitaBreath is not intended as a NIV device and is limited to intermittent use for single breaths via mouthpiece but shows value in recovering from shortness of breath during physical activity and may assist with increasing patient endurance to perform daily activities as opposed to pursed lip breathing alone. Device is easy to use without concomitant services to monitor patient use with the advantage of portability. Settings are pre-set at 18/6 cmH2O and are non-adjustable. Consideration should be given to a portable NIV with nasal interface to reduce breathlessness during exercise.*

REFERENCE: Vogiatzis I, Chynkiamis N, Armstrong M, et al. Intermittent Use of Portable NIV Increases Exercise Tolerance in COPD: A Randomised, Cross-Over Trial. *J Clin Med.* 2019;8(1):94.

2. Physiologic effects of an ambulatory ventilation system in chronic obstructive pulmonary disease (2013)

METHODS: Fifteen men with COPD ($FEV1 = 32.2 \pm 12.0\%$ predicted; $FEV1/FVC = 31.6 \pm 7.1\%$; exercise oxygen saturation as measured by pulse oximetry $[SpO_2] = 86.5\% \pm 2.9\%$) participated. After incremental testing establishing peak work rate, subjects completed three visits in which they performed CWR exercise to tolerance at 80% peak workrate: (1) unencumbered breathing room air, (2) using NIOV + compressed air, (3) using NIOV + compressed O₂, or (4) using O₂ via nasal cannula. Assessments included exercise duration, surface inspiratory muscle EMG, SpO₂, transcutaneous PCO₂, and Borg dyspnea scores.

RESULTS: Exercise endurance was 17.6 6 5.7 minutes using NIOV + O₂, greatly prolonged compared with unencumbered (5.6 ± 1.9 min), nasal O₂ (11.4 ± 6.8 min), and NIOV + Air (6.3 ± 4.1 min). Isotime SpO₂ was higher and intercostal, scalene, and diaphragmatic EMG activity was reduced using NIOV + O₂ compared with unencumbered, nasal O₂, and NIOV + Air, signifying respiratory muscle unloading. Isotime dyspnea reduction correlated with isotime EMG reduction ($r = 0.42$, $P = 0.0053$). There were no significant differences in isotime VD/VT or transcutaneous PCO₂ among treatments.

CONCLUSION: NIOV + O₂ yielded substantial exercise endurance improvements accompanied by respiratory muscle unloading and dyspnea reductions in patients with severe hypoxemic COPD.

DISCUSSION: *Small sample size but good results showing value of portable NIV.*

REFERENCE: Porszasz J, Cao R, Morishige R, van Eykern LA, Stenzler A, Casaburi R. Physiologic effects of an ambulatory ventilation system in chronic obstructive pulmonary disease. *Am J Respir Crit Care Med.* 2013;188(3):334-342.

3. Home noninvasive positive pressure ventilation with built-in software in stable hypercapnic COPD: a short-term prospective, multicenter, randomized, controlled trial (2017)

METHODS: The current multicenter prospective, randomized, controlled trial enrolled patients with stable GOLD stages III and IV hypercapnic COPD. Patients were randomly assigned via a computer-generated randomization sequence, with a block size of four patients, to continue optimized treatment (control group) or to receive additional NPPV (intervention group) for 3 months. The primary outcome was arterial carbon dioxide pressure (PaCO₂). Data were derived from built-in software and analyzed every 4 weeks. Analysis was carried out with the intention to treat. This study is registered with ClinicalTrials.gov, number NCT02499718.

RESULTS: Patients were recruited from 20 respiratory units in China from October 1, 2015, and recruitment was terminated with a record of the vital statistics on May 31, 2016. A total of 115 patients were randomly assigned to the NPPV group (n=57) or the control group (n=58). Patients complied well with NPPV therapy (mean [± standard deviation] day use 5.6±1.4 h). The mean estimation of leaks was 37.99±13.71 L/min. The changes in PaCO₂ (-10.41±0.97 vs -4.32±0.68 mmHg, P=0.03) and 6-min walk distance (6MWD) (38.2% vs 18.2%, P=0.02) were statistically significant in the NPPV group versus the control group. COPD assessment test (CAT) showed a positive trend (P=0.06) in favor of the NPPV group. Pulmonary function and dyspnea were not different between groups.

CONCLUSION: Ventilators equipped with built-in software provided methodology for monitoring NIV use at home, which could facilitate the improvement of compliance and quality control of NIV use. It was shown that three months use of NIV at home could reduce the PaCO₂ and improve exercise tolerance (6MWD) in chronic hypercapnic COPD patients.

DISCUSSION: Strong evidence, good data supporting home NIV use.

REFERENCE: Zhou L, Li X, Guan L, et al. Home noninvasive positive pressure ventilation with built-in software in stable hypercapnic COPD: a short-term prospective, multicenter, randomized, controlled trial. *Int J Chron Obstruct Pulmon Dis*. 2017;12:1279-1286. Published 2017 Apr 27.

4. Effects of a Highly Portable Noninvasive Open Ventilation System on Activities of Daily Living in Patients with COPD (2015)

METHODS: Patients with stable, oxygen-dependent COPD were recruited for this prospective, open-label, crossover study. Inclusion criteria included supplemental oxygen use, elevated dyspnea score, and the ability to perform ADLs. Patients performed a selected ADL for as long as tolerable while using standard oxygen therapy. Following a rest period, the same ADL was repeated using the NIOV system. ADL endurance time, oxyhemoglobin saturation measured by pulse oximeter (SpO₂), dyspnea, fatigue, and discomfort scores were recorded.

RESULTS: Thirty patients were enrolled and 29 patients completed the study. Mean ADL endurance increased by 85% (13.4 vs. 7.2 min) using NIOV compared with oxygen therapy (p<0.0001). Mean SpO₂ was significantly higher during ADLs using NIOV versus oxygen therapy (p<0.0001). Median dyspnea, fatigue, and discomfort scores were significantly lower using NIOV during ADLs compared to oxygen therapy (p<0.01). No device-related adverse events were observed.

CONCLUSIONS: This study demonstrated that a novel, portable noninvasive open ventilation system can improve ADL performance in the home setting. Compared to standard oxygen therapy, the NIOV system provided statistically clinically significant increases in ADL endurance time and oxygenation, while decreasing dyspnea, fatigue, and discomfort. The NIOV system appears to offer a practical option for increasing activity and exercise tolerance in oxygen-dependent patients with COPD.

COMMENTS: *Small study but good statistical results. The portability of this device and ease of use is an advantage for patient mobility and physical activity endurance which can greatly improve a patient's quality of life, independence, and overall physical fitness.*

REFERENCE: Carlin BW, Wiles KS, McCoy RW, Brennan T, Easley D, Thomashow RJ. Effects of a Highly Portable Noninvasive Open Ventilation System on Activities of Daily Living in Patients with COPD. *Chronic Obstr Pulm Dis.* 2015;2(1):35-47.

5. Two-year home-based nocturnal noninvasive ventilation added to rehabilitation in chronic obstructive pulmonary disease patients: A randomized controlled trial (2011)

METHODS: Sixty-six patients could be analyzed for the two-year home-based follow-up period. The study design was randomized controlled with parallel groups. Patients were assigned to nocturnal NIPPV in addition to rehabilitation (NIPPV + PR) or to rehabilitation alone (PR). After completing 12-week inpatient pulmonary rehab program patients completed a home-based community PR program 1-2 days a week. Differences in change between the NIPPV + PR and PR group were assessed by a linear mixed effects model with a random effect on the intercept, and adjustment for baseline values. The primary outcome was health-related quality of life (HRQL); secondary outcomes were mood state, dyspnea, gas exchange, functional status, pulmonary function, and exacerbation frequency.

RESULTS: Although the addition of NIPPV did not significantly improve the Chronic Respiratory Questionnaire compared to rehabilitation alone (mean difference in change between groups -1.3 points (95% CI: -9.7 to 7.4)), the addition of NIPPV did improve HRQL assessed with the Mageri Respiratory Failure questionnaire (-13.4% (-22.7 to -4.2; $p = 0.005$)), mood state (Hospital Anxiety and Depression scale -4.0 points (-7.8 to 0.0; $p = 0.05$)), dyspnea (Medical Research Council -0.4 points (-0.8 to -0.0; $p = 0.05$)), daytime arterial blood gases (PaCO₂ -0.4 kPa (-0.8 to -0.2; $p = 0.01$); PaO₂ 0.8 kPa (0.0 to 1.5; $p = 0.03$)), 6-minute walking distance (77.3 m (46.4 to 108.0; $p < 0.001$)), Groningen Activity and Restriction scale (-3.8 points (-7.4 to -0.4; $p = 0.03$)), and forced expiratory volume in 1 second (115 ml (19 to 211; $p = 0.019$)). Exacerbation frequency was not changed.

CONCLUSIONS: The addition of NIPPV to pulmonary rehabilitation for 2 years in severe COPD patients with chronic hypercapnic respiratory failure improves HRQL mood, dyspnea, gas exchange, exercise tolerance and lung function decline. The benefits increase further with time.

COMMENTS: *Some patients participated in the home-based community PR program 1 day per week and others participated 2 days per week which could affect the results. Many patients do not have the support or resources to attend outpatient pulmonary rehab in the community. The addition of portable NIV devices (pNIV, NIOV) can add value to disease management in these patients to promote physical activity and increase endurance.*

REFERENCE: Duiverman ML, Wempe JB, Bladder G, et al. Two-Year home-based nocturnal noninvasive ventilation added to rehabilitation in chronic obstructive pulmonary disease patients: a randomized controlled trial. *Respir Res* 2011;12:9921-12.

6. Noninvasive Ventilation as an Important Adjunct to an Exercise Training Program in Subjects With Moderate to Severe COPD (2018)

METHODS: 47 subjects with COPD who were enrolled in a physical training program were randomized to either physical training alone or NIV physical training (NIV-Physical training). Physical training consisted of dynamic aerobic exercises on a treadmill 3 times/week for 6 weeks, for a total of 18 sessions. NIV was titrated according to the subject's tolerance at rest and during exercise. Assessments included physiological responses and symptoms at the incremental

cardiopulmonary exercise test peak and during submaximal exercise on a treadmill, 6-min walk distance, maximum inspiratory (P_Imax) and expiratory pressure (P_Emax), BODE index, and health-related quality of life.

RESULTS: 43 subjects completed the 6-week physical training program. Both groups improved 6-min walk distance, P_Imax, BODE index, and quality of life, and no differences were found between groups. However, significant improvements were observed for subjects in the NIV Physical training group with regard to P_Emax, maximum V̇ O₂, maximum metabolic equivalents, circulatory power, and maximum SpO₂.

CONCLUSIONS: A 6-week physical training program alone can improve tolerance for exercise and quality of life, in addition to reducing the risk of mortality. However, NIV associated with a physical training program was shown to have an additive beneficial effect on powerful prognostic markers (maximum V̇ O₂ and circulatory power) and to reduce symptoms and improve oxygen saturation in subjects with moderate to very severe COPD. From a clinical perspective, our data indicate that strategies aimed at reducing work of breathing, such as NIV, can have additional beneficial effects on important physiological markers and symptoms during exercise in this population.

COMMENTS: *As expected, NIV increased physical activity endurance and reduced work of breathing but offers no portability to increase physical activities. Respironics BiPAP-S was used with initial settings of 6/3 cmH₂O and titrated based on patient tolerance and work of breathing with no clinical parameters measured. Portable NIV devices would be beneficial for this population of patients.*

REFERENCE: Marrara KT, Di Lorenzo VAP, Jaenisch RB, et al. Noninvasive Ventilation as an Important Adjunct to an Exercise Training Program in Subjects With Moderate to Severe COPD. *Respir Care*. 2018;63(11):1388-1398.

7. Home initiation of chronic non-invasive ventilation in COPD patients with chronic hypercapnic respiratory failure: a randomised controlled trial (2020)

METHODS: Sixty-seven stable hypercapnic COPD patients were randomised to initiation of NIV in the hospital or at home using telemedicine. Primary outcome was daytime arterial carbon dioxide pressure (PaCO₂) reduction after 6 months NIV, with a non-inferiority margin of 0.4 kPa. **Secondary outcomes** were health-related quality of life (HRQoL) and costs.

RESULTS: Home NIV initiation was non-inferior to in-hospital initiation (adjusted mean difference in PaCO₂ change home vs in-hospital: 0.04 kPa (95% CI -0.31 to 0.38 kPa), with both groups showing a PaCO₂ reduction at 6 months compared with baseline (home: from 7.3±0.9 to 6.4±0.8 kPa (p<0.001) and in-hospital: from 7.4±1.0 to 6.4±0.6 kPa (p<0.001)). In both groups, HRQoL improved without a difference in change between groups (Clinical COPD Questionnaire total score-adjusted mean difference 0.0 (95% CI -0.4 to 0.5)). Furthermore, home NIV initiation was significantly cheaper (home: median €3768 (IQR €3546–€4163) vs in-hospital: median €8537 (IQR €7540–€9175); p<0.001).

CONCLUSION: This is the first study showing that home initiation of chronic NIV in stable hypercapnic COPD patients, with the use of telemedicine, is non-inferior to in-hospital initiation, safe and reduces costs by over 50%.

COMMENTS: *Study shows NIV can be safely and equally managed at home vs in-hospital, reduce costs, and improve the patient's quality of life. Home NIV use can greatly reduce the burden on the healthcare system by reducing hospital admissions and ER visits. Long term home NIV use should be monitored and evaluated by a qualified respiratory therapist (RT) initially but frequency of RT visits could be decreased when patient compliance is established. Telemedicine visits are a good cost saving alternative for follow up, as well.*

REFERENCE: Duiverman ML, et al. *Thorax*. 2020; Vol.75:244–252.

8. Comparison of exercise capacity in COPD and other etiologies of chronic respiratory failure requiring non-invasive mechanical ventilation at home: retrospective analysis of 1-year follow-up (2015)

METHODS: This retrospective cohort study was conducted in a tertiary pulmonary disease hospital in patients who had completed 1-year follow-up under home NIMV because of CHRf with different etiologies (ie, chronic obstructive pulmonary disease [COPD], obesity hypoventilation syndrome [OHS], kyphoscoliosis [KS], and diffuse parenchymal lung disease [DPLD]), between January 2011 and January 2012. The results of arterial blood gas (ABG) analyses and spirometry, and 6MWD measurements with 12-month interval were recorded from the patient files, in addition to demographics, comorbidities, and body mass indices. The groups were compared in terms of 6MWD via analysis of variance (ANOVA) and multiple linear regression (MLR) analysis (independent variables: analysis age, sex, baseline 6MWD, baseline forced expiratory volume in 1 second, and baseline partial carbon dioxide pressure, in reference to COPD group).

RESULTS: A total of 105 patients with a mean age (\pm standard deviation) of 61 ± 12 years of whom 37 had COPD, 34 had OHS, 20 had KS, and 14 had DPLD were included in statistical analysis. There were no significant differences between groups in the baseline and delta values of ABG and spirometry findings. Both univariate ANOVA and MLR showed that the OHS group had the lowest baseline 6MWD and the highest decrease in 1 year (linear regression coefficient -24.48 ; 95% CI -48.74 to -0.21 , $P=0.048$); while the KS group had the best baseline values and the biggest improvement under home NIMV (linear regression coefficient 26.94 ; 95% CI -3.79 to 57.66 , $P=0.085$).

COPD patients had significantly higher post-test scores for dyspnea noted during the 1-year 6MWD compared with patients with other underlying diagnoses [median 3 (1–5) vs 1 (0–2) for each other diagnosis, $P=0.003$]. However, no other significant differences were noted between the diagnostic groups in terms of pre- and post-test VAS-F and dyspnea scores during the baseline and 1-year 6MWT.

No significant difference was noted in terms of emergency admission, hospital stay, and the interval between the last exacerbation and 1-year assessment in the patients who were clinically stable but with different underlying diagnoses.

CONCLUSION: The 6MWD measurements revealed improvement in exercise capacity test in CHRf patients with COPD receiving home NIMV treatment. Home NIMV devices were prescribed according to home mechanical ventilation guidelines after a good response was achieved with NIMV during the ICU stay. All patients had home NIMV via a bi-level positive airway pressure (BiPAP) machine in a spontaneous/timed (S/T) mode with an oronasal interface. Treatment efficacy was assessed by clinical status and ABG measurements. Inspiratory positive airway pressure (IPAP) and expiratory positive airway pressure (EPAP) values of NIMV devices were titrated and recorded.

Table 1 Baseline characteristics of chronic respiratory failure patients having non-invasive ventilation at home followed at the outpatient clinic between 2011 and 2012

	COPD, n=37	OHS, n=34	Kyphoscoliosis, n=20	DPLD, n=14
Age, years, mean \pm SD	65 \pm 10	65 \pm 8	46 \pm 10	62 \pm 12
Female, %	8.1	50	45	21.4
BMI, kg/m ² , mean \pm SD	25 \pm 6	41 \pm 6	27 \pm 7	27 \pm 6
HNIV parameters, mean \pm SD				
IPAP, cm H ₂ O	24 \pm 3	23 \pm 3	22 \pm 5	21 \pm 5
EPAP, cm H ₂ O	5.3 \pm 0.7	5.8 \pm 0.8	5.3 \pm 0.6	5.5 \pm 0.7
Therapy duration, hour/day	6.7 \pm 1.9	6.4 \pm 2.4	5.9 \pm 1.8	5.8 \pm 1.4
Charlson comorbidity index, mean \pm SD	4 \pm 1	4 \pm 1	2 \pm 2	3 \pm 1

Abbreviations: BMI, body mass index; COPD, chronic obstructive lung disease; DPLD, diffuse parenchymal lung disease; EPAP, expiratory positive airway pressure; HNIV, home non-invasive ventilation; IPAP, inspiratory positive airway pressure; OHS, obesity hypoventilation syndrome; SD, standard deviation.

COMMENTS: All diagnosis groups were compared to the COPD group (as the reference) but this study did show improvement in the COPD group. Home NIV settings were determined in the hospital prior to discharge to home for continued NIV use with an average of 6.7 hour/day which indicates good patient compliance.

REFERENCE: Salturk, C. et al; International Journal of COPD; Nov 2015:10 2559–2569

PATIENT SELECTION, VENTILATOR SETTINGS AND INTERFACES:

1. Home noninvasive ventilatory support for patients with chronic obstructive pulmonary disease: patient selection and perspectives (2018)

INTRODUCTION: A systemic review and data meta-analysis from 2014 concluded that there was not enough evidence at the time to support the routine use of Home-NIV in patients with stable hypercapnic COPD.³ Remarkably, this is in clear contrast to clinical practice, where Home-NIV for chronic hypercapnic COPD has been a well-established treatment in many European countries during at least the last two decades.^{2,4} Furthermore, this topic has received a high amount of scientific attention, as demonstrated by the number of recent studies related to COPD patients and long-term NIV following acute hypercapnic respiratory failure^{5,6} and chronic hypercapnic respiratory failure.^{7,8} Patients with chronic hypercapnic respiratory failure (type II) are the subgroup of COPD patients most likely to benefit from Home-NIV. There is now increasing scientific evidence support a number of indications for Home-NIV in patients suffering from chronic hypercapnic COPD (Table 1).

Table 1 Recommendations for Home-NIV in chronic hypercapnic respiratory failure and COPD based on scientific as well as clinical-guided perspectives

Chronic hypercapnic COPD		
Hypercapnia*	Daytime PaCO ₂ ≥50 mmHg (≥6.67 kPa) Nocturnal PaCO ₂ ≥55 mmHg (≥7.33 kPa) Daytime PaCO ₂ 46–50 mmHg (6.13–6.67 kPa)	or or and an increase in nocturnal PtcCO ₂ of 10 mmHg (1.33 kPa)
Following acute exacerbation with need for mechanical ventilation		
Persistent hypercapnia*	14–28 days following acute NIV due to respiratory acidosis	Daytime PaCO ₂ >53 mmHg (≥7.07 kPa)
Weaning failure**	Following mechanical ventilation (NIV or invasive ventilation) in hospital	and persistent ventilatory failure without NIV

Notes: *Represents scientific perspectives and **represents clinical-guided perspectives. Data from Windisch et al,¹ Crimi et al,² Struik et al,³ Murphy et al,⁴ Köhnlein et al,⁷ Windisch et al,⁹ and Schönhofer et al.¹⁰

Abbreviations: Home-NIV, home mechanical noninvasive ventilation; PaCO₂, arterial pressure of carbon dioxide; PtcCO₂, transcutaneous pressure of carbon dioxide.

Ventilator settings and compliance: Besides the abovementioned issues of patient selection, adequate establishment of ventilator settings and targets for Home-NIV are thought to play a substantial role in treatment success.^{1,19} Table 2 summarizes the ventilator settings, interface selection, and compliance data associated with the most important Home-NIV trials on chronic hypercapnic COPD patients;^{5–8,11–13} this summary demonstrates that different approaches to ventilator settings have been used over the last two decades.

Table 2 Ventilator settings used in long-term randomized controlled trials on Home-NIV therapy for chronic hypercapnic COPD patients

Study (year)	Patients ^a	Mean IPAP/EPAP	Mode; mean backup rate	Interface	Compliance
Casanova et al ¹¹	N=44	12/4 cm H ₂ O	Spontaneous mode; n/a	Nasal mask	6.2 hours/day at 3 and 6 months; 5.9 hours/day after 12 months
Clini et al ¹²	N=86	14/2 cm H ₂ O	Spontaneous/timed mode; n/a	Nasal mask	9 hours/day
McEvoy et al ¹³	N=144	13/5 cm H ₂ O	n/a	Nasal or full-face mask, according to patient comfort	n/a
Duiverman et al ⁸	N=72	23/6 cm H ₂ O	Spontaneous/timed mode; 18 breaths/min	Nasal, oronasal	6.9 hours/night at 24 months
Köhnlein et al ⁷	N=195	22/5 cm H ₂ O	Controlled or assisted pressure support; 16 breaths/min	n/a	5.9 hours/day
Struik et al ⁵	N=201	19/5 cm H ₂ O	Spontaneous/timed mode; 15 breaths/min	Full-face mask (exception for 1 patient with total face mask)	6.3 hours/night

Selection of interface: In contrast to the topic of ventilator settings, the basis for selecting the appropriate ventilation interface has only so far received limited scientific attention.^{36,37} This is somewhat surprising because the type of interface has been reported to be crucial for the success of NIV therapy in the acute and chronic settings.³⁸ In most of the studies discussed here, mask selection was based on patient comfort and/or the recommendation provided by the supervising ventilation center (Table 2). There is a broad variety of interfaces available, including nasal masks, oronasal masks, total face masks, or mouth pieces, depending on patient needs and ventilation strategies.³⁶

CONCLUSION: Home-NIV for patients with end-stage COPD has become a well-established form of therapy over the last few decades, despite a lack of consensus among the corresponding scientific literature. However, recent research trials have provided evidence that Home-NIV is associated with long-term survival benefits as well as improvements in HRQL, gas exchange, and lung function. These positive results were first observed in the stable hypercapnic COPD patient subgroup. Accordingly, a current study reported similar positive effects of Home-NIV therapy in this particular subgroup of COPD patients who suffer from an acute exacerbation that requires mechanical ventilation therapy and is accompanied by persistent hypercapnia – a generally severe event that is associated with a poor prognosis.

DISCUSSION: *This is a great commentary and perspective regarding home NIV use in COPD patients with CRF and contains excellent references to support recommendations. In addition being able to provide NIV at lower pressures and lower flows would be very beneficial.*

REFERENCE: Storre, et al; Home noninvasive ventilatory support for patients with chronic obstructive pulmonary disease: patient selection and perspectives. *International Journal of COPD*. 2018;13:753–760.

2. Interfaces and ventilator settings for long-term noninvasive ventilation in COPD patients (2017)

METHOD: Ventilator settings and NIV compliance were assessed in this prospective cross-sectional monocentric cohort study of COPD patients with pre-existing NIV. Daytime arterialized blood gas analyses and lung function testing were also performed. The primary end point was the distribution among study patients of interfaces (full-face masks [FFMs] vs nasal masks [NMs]) in a real-life setting.

RESULTS: The majority of the 123 patients studied used an FFM (77%), while 23% used an NM. Ventilation settings were as follows: mean \pm standard deviation (SD) inspiratory positive airway pressure (IPAP) was 23.2 \pm 4.6 mbar and mean \pm SD breathing rate was 16.7 \pm 2.4/minute. Pressure support ventilation (PSV) mode was used in 52.8% of patients, while assisted pressure-controlled ventilation (aPCV) was used in 47.2% of patients. Higher IPAP levels were associated with an increased use of FFMs (IPAP 21 mbar: 73% vs IPAP 25 mbar: 84%). Mean compliance was 6.5 hours/day, with no differences between FFM (6.4 hours/day) and NM (6.7 hours/day) users. PaCO₂ assessment of ventilation quality revealed comparable results among patients with FFMs or NMs.

CONCLUSION: This real-life trial identified the FFM as the predominantly used interface in COPD patients undergoing long-term NIV. The increased application of FFMs is, therefore, likely to be influenced by higher IPAP levels, which form part of the basis for successful application of HI-NIV in clinical practice.

COMMENTS: *Successful NIV use can greatly depend on the selection of interfaces available for optimal patient comfort and compliance. Ventilator settings and interface for NIV are patient specific and should be targeted for patient comfort and tolerance, optimal settings to unload respiratory muscles, reduce PCO₂ and improve patient compliance to achieve optimal outcomes. Titrating NIV settings, providing mask options for optimal fit, and monitoring compliance should initially be performed by a qualified respiratory therapist for home NIV use.*

REFERENCE: Callegari, J, et al. Interfaces and ventilator settings for long-term noninvasive ventilation in COPD patients. International Journal of COPD 2017;12 1883–1889.