Etude descriptive transversale multicentrique concernant l'organisation actuelle de la ventilation non-invasive sur les Cantons de Genève et Vaud : mise à jour de la "Geneva Lake Study"

Cantero, Chloé

CHEST

Long-Term Noninvasive Ventilation in the Geneva Lake Area

Indications, Prevalence, and Modalities

Chloé Cantero, MD; Dan Adler, MD; Patrick Pasquina; Christophe Uldry, MD; Bernard Egger, MD; Maura Prella, MD; Alain B. Younossian, MD; Paola M. Soccal, MD; Jean-Louis Pépin, MD; and Jean-Paul Janssens, MD

BACKGROUND: Noninvasive ventilation (NIV) is standard of care for chronic hypercapnic respiratory failure, but indications, devices, and ventilatory modes are in constant evolution.

RESEARCH QUESTION: To describe changes in prevalence and indications for NIV over a 15-year period; to provide a comprehensive report of characteristics of the population treated (age, comorbidities, and anthropometric data), mode of implementation and follow-up, devices, modes and settings used, physiological data, compliance, and data from ventilator software.

STUDY DESIGN AND METHODS: Cross-sectional observational study designed to include all subjects under NIV followed by all structures involved in NIV in the Cantons of Geneva and Vaud (1,288,378 inhabitants).

RESULTS: A total of 489 patients under NIV were included. Prevalence increased 2.5-fold since 2000 reaching 38 per 100,000 inhabitants. Median age was 71 years, with 31% being $>$ 75 years of age. Patients had been under NIV for a median of 39 months and had an average of 3 $\pm$ 1.8 comorbidities; 55% were obese. COPD (including overlap syndrome) was the most important patient group, followed by obesity hypoventilation syndrome (OHS) (26%). Daytime $Paco_2$ was most often normalized. Adherence to treatment was satisfactory, with 8% only using their device $<$ 3.5 h/d. Bilevel positive pressure ventilators in spontaneous/timed mode was the default mode (86%), with a low use of autotitrating modes. NIV was initiated electively in 50% of the population, in a hospital setting in 82%, and as outpatients in 15%.

INTERPRETATION: Use of NIV is increasing rapidly in this area, and the population treated is aging, comorbid, and frequently obese. COPD is presently the leading indication followed by OHS.

TRIAL REGISTRY: ClinicalTrials.gov; No.: NCT04054570; URL: www.clinicaltrials.gov

CHEST 2020; 158(1):279-291

KEY WORDS: compliance; COPD; hypoventilation syndrome; monitoring; noninvasive ventilation; obesity; hypoventilation syndrome; prevalence; ventilator settings

FOR EDITORIAL COMMENT, SEE PAGE 26

ABBREVIATIONS: ABG = arterial blood gas; AHI = apnea-hypopnea index; ASV = adaptive servo-ventilation; EPAP = expiratory positive airway pressure; IPAP = inspiratory positive airway pressure; IQR = interquartile range; KYPH = kyphoscoliosis; NIV = noninvasive ventilation; NMD = neuromuscular disease; OHS = obesity hypoventilation syndrome; OSAS = OSA syndrome; RLD = restrictive lung disorder; SRBD = sleep-related breathing disorder

AFFILIATIONS: From the Division of Pulmonary Diseases (Drs Cantero, Adler, Soccal, and Janssens; and Mr Pasquina), Geneva University Hospitals (HUG), Geneva, Switzerland; the Faculty of Medicine (Drs Adler, Soccal, and Janssens), University of Geneva, Geneva, Switzerland; the Division of Pulmonary Diseases and Pulmonary Rehabilitation Center (Drs Uldry and Egger), Rolle Hospital, Rolle, Vaud, Switzerland; the Division of Pulmonary Diseases (Dr Prella),

Noninvasive ventilation (NIV) is accepted as standard of care for chronic hypercapnic respiratory failure. NIV appeared in Western Europe and in the United States in the mid-1980s shortly after the advent of CPAP for severe OSA syndrome (OSAS).[1,2] Ventilators used for home ventilation were initially volume-cycled devices.[3] A major breakthrough in chronic NIV was the advent of a simple bilevel positive pressure ventilator device for home use commercialized in 1990.[4,5] During the 1990s, pressure-cycled ventilators progressively replaced the more cumbersome, expensive, and less comfortable volume-cycled devices.[3]

Over the past 15 years, home ventilators have undergone major technical evolutions; however, sometimes they are of undetermined clinical relevance.[6-8] Volume-assured pressure support, autotitrating expiratory positive airway pressure (EPAP), inspiratory positive airway pressure (IPAP), pressure support, backup rates, and built-in algorithms profiled for certain pathologies are now standard options on many ventilators.[9-15] More importantly, built-in software provides important information for monitoring efficacy of NIV (ie, estimation of leaks, tidal volume, residual respiratory events, percentage of cycles triggered and cycled by the ventilator, compliance).[16,17]

The population of patients under chronic NIV has also changed, from the initial predominantly restrictive indications (sequelae of TB, postpolio syndrome, chest wall disorders, and neuromuscular disorders) to a progressive increase of patients with chronic respiratory failure (CRF) because of obesity hypoventilation syndrome (OHS), COPD, and overlap syndromes which started in the late 1990s.[3,18,19]

Fifteen years after our initial cohort study,[3] this report provides a comprehensive description of all patients under home mechanical ventilation in the Cantons of Geneva and Vaud, an area covering a population of around 1.3 million inhabitants. The aims of this study were as follows: (1) to detail present indications for NIV, their relative importance, and the prevalence of its use; (2) to describe the population under NIV, and its major comorbidities; (3) to compare prevalence of NIV and indications with data previously published by our group covering the same area and population 15 years ago; and (4) to provide detailed data on settings, compliance, correction of respiratory events and other items reported by ventilator software, and modalities of medical follow-up.

Patients and Methods

Study Design

A cross-sectional observational study was designed to include all subjects under NIV followed by every possible structure involved in NIV in the Cantons of Geneva and Vaud (1,288,378 inhabitants in 2017): university hospitals, regional general hospitals, pulmonary rehabilitation centers, and pulmonologists in private practice. Prevalence was compared with data previously published by our group covering the same area and population in 2000.[3]

In Switzerland, home mechanical ventilation can be prescribed, initiated, and followed by pulmonologists in private practice without referral to an expert center.

Ethical Approval

Ethical approval was granted by the Cantonal Commission for Research Ethics in Geneva, Switzerland (No. PB_2016-00925/15-275) in agreement with the amended Declaration of Helsinki. The trial was registered at clinicaltrials.gov (No. NCT04054570). Identification, screening, and data collection were performed by two investigators between June 1, 2016, and July 10, 2018.

Inclusion/Exclusion Criteria

This study focuses exclusively on patients treated by pressure-cycled, multimodal, and volume-cycled home ventilators, excluding adaptive servo-ventilation (ASV), at home or in a long-term care facility (not a hospital) for ≥ 3 months. Patients were excluded if they used any other device, if they refused data collection regarding their home NIV, or if their pulmonologist refused to participate in this study.

Data Collected

Anthropometric data, diagnoses leading to NIV, a list of predefined major comorbidities, pulmonary function tests, arterial blood gases (ABGs), pulse oximetry, transcutaneous capnography, type of NIV devices, settings, interfaces, and reports downloaded from devices were collected from medical records. Modalities of implementation of NIV (elective vs emergency, outpatient vs inpatient, by a hospital vs a pulmonologist) and follow-up were also collected. No additional investigation was performed by the investigators. Availability of recent pulmonary function tests, ABGs, pulse-oximetry, and

Lausanne University Hospital (CHUV), Lausanne, Switzerland; the Division of Pulmonary Diseases and Intensive Care (Dr Younossian), La Tour Hospital, Meyrin, Geneva, Switzerland; the HP2 laboratory (Dr Pépin), Inserm U1042 unit, University Grenoble Alps, Grenoble, France; and the EFCR laboratory (Dr Pépin), Thorax and vessels, Grenoble Alps University Hospital, Grenoble, France.

FUNDING/SUPPORT: This study received financial support from the "Ligue Pulmonaire Genevoise" (www.lpge.ch) a nonprofit home care provider for respiratory care.

CORRESPONDENCE TO: Jean-Paul Janssens, MD, Division of Pulmonary Diseases, Geneva University Hospital, 4-6 Rue Gabrielle-Perret-Gentil, 1211 Geneva 14, Switzerland; e-mail: jean-paul.janssens@hcuge.ch

DOI: https://doi.org/10.1016/j.chest.2020.02.064

capnography depended on real-life follow-up procedures and medical records. ABG measurements were all performed without NIV and are follow-up values. Data recorded were the most recent measurements performed within the 12 months prior to data collection. Tests which had not been performed within the previous 12 months were considered as missing.

To ensure that data collected were comprehensive, we cross-checked lists provided by all health-care providers in our area, ventilator manufacturers, and hospitals involved. Screening and data collection started on June 1, 2016, and ended on July 10, 2018.

Diagnostic Categories

Diagnostic and functional criteria used for determining indication for NIV were always determined by pulmonologists either electively, or after an acute episode of hypercapnic respiratory failure (this is a prerequisite for reimbursement).

For all patients, indication for implementing NIV was based on the 1999 Consensus Conference Report.[20] Patients with COPD had persistent airflow limitation with a documented $FEV_1/FVC < 70\%$ after bronchodilation (according to www.goldcopd.org criteria). NIV was implemented if patients with COPD were hypercapnic (> 7.3 kPa or 55 mm Hg) in a stable condition, if they remained hypercapnic after an acute episode of hypercapnic respiratory failure, or if they were hypercapnic (50-54 mm Hg) and had repeated episodes of acute episode of hypercapnic respiratory failure (≥ 2) within the preceding year. Patients with overlap syndrome had COPD and OSAS. Patients with OHS, defined as the combined presence of obesity (BMI > 30 kg/m^2) and daytime hypercapnia in the absence of any other causes of restrictive or obstructive pulmonary disorder, were treated by NIV when $Paco_2$ was > 45 mm Hg.[21] Details regarding neuromuscular diseases (NMDs), kyphoscoliosis (KYPH), other restrictive lung disorders (RLDs), and sleep-related breathing disorders (SRBDs) are provided in Table 2 and e-Table 2. For patients with RLDs and KYPH, NIV was initiated in the presence of symptoms and a daytime $Paco_2$ > 45mm Hg. For patients with SRBDs, NIV was most often implemented after failure of CPAP or ASV.

Sleep studies are not mandatory for indications such as RLDs, KYPH, or COPD without overlap syndrome. Respiratory polygraphy or polysomnography are usually performed in patients with OHS, SRBD, and overlap syndrome.

Statistical Analysis

Qualitative data were described as frequencies and percentages, and quantitative data were described as medians and interquartile ranges (IQRs (25th-75th percentiles) or means and SDs as appropriate.

Association between choice of interface and apnea-hypopnea index (AHI) was assessed using a simple linear regression model. Mean differences of number of comorbidities, average daily use of ventilator, and correction of SRDBs between subjects with a hospital-based or a liberal pulmonologist-based follow-up were assessed using Welch and Student *t* tests. A multivariable linear regression model was used to investigate the effect of potential factors impacting on the average daily use of NIV.

Missing data were simply reported as a modality of follow-up reflecting real-life practices. All analyses were performed on a two-sided alpha level of 0.05.

Results

Two university hospitals, one regional general hospital, one pulmonary rehabilitation center, and 38 of the 43 pulmonologists in private practice in the Cantons of Geneva and Vaud participated in data collection (ie, all possible structures and specialists involved, albeit for five pulmonologists).

Of the 1,014 patients identified as being treated by home NIV during the data collection period, 489 patients under NIV were included in this analysis (Fig 1).

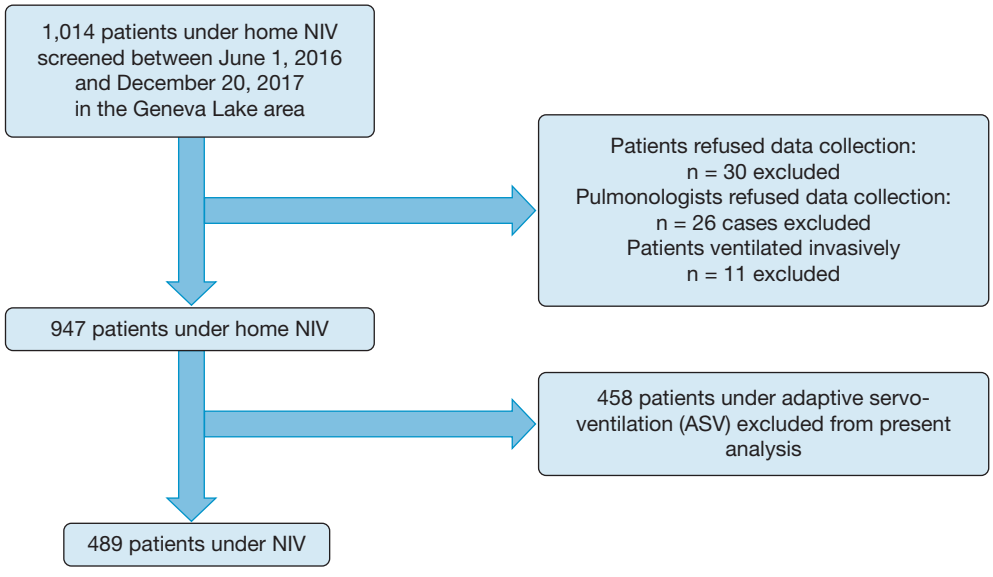

Figure 1 – *Flowchart. NIV = noninvasive ventilation.*

Patients under ASV (n = 458) and patients who were ventilated by tracheostomy (n = 11) were excluded (this number has remained stable over the past 15 years).

Based on a population of 1,288,378 inhabitants at the end of 2017 in this area, prevalence of NIV can be estimated at 37.9 per 100,000 inhabitants. This represents a 2.5-fold increase when compared with the 154 patients under NIV in the same area in 2000 (ie, a prevalence of 15.1 per 100,000 inhabitants).[3] Changes in diagnostic categories since 2000 are shown in Figure 2. Details of these changes are provided in e-Table 1.

Study Population and Comorbidities

Details as to specific diagnoses of patient groups included in Tables 1 and 3-5 are provided in Tables 2 and e-Table 2.

Median age (71 years; IQR, 59-77) was rather high: 151 subjects (31%) were ≥ 75 years of age and 88 (18%) were ≥ 80 years of age. There was a slight male predominance (n = 272; 56%). The youngest group was that of patients with NMDs.

Patients had been under NIV for a median of 39 months (IQR, 14-73).

Comorbidities and their respective prevalence are shown in Table 1 and e-Figure 1. On average, patients had 3.0 ± 1.8 comorbidities: 91% had at least one comorbidity, 77% at least two comorbidities, and 60% had three or more comorbidities. Systemic hypertension (n = 334; 68%) was the most frequent comorbidity reported. Obesity was highly prevalent: BMI was ≥ 30 kg/m^2 in 270 patients (55%), ≥ 35 kg/m^2 in 180 patients (37%), and ≥ 40 kg/m^2 in 106 patients (22%).

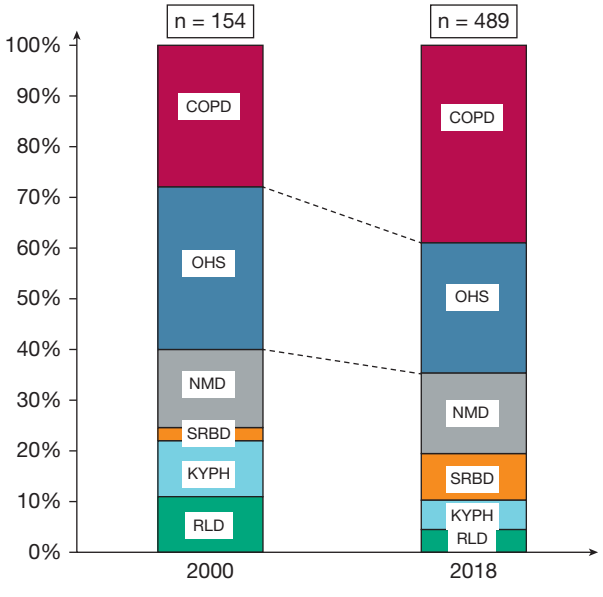

Figure 2 – *Evolution of indications for noninvasive ventilation in the Geneva Lake area between 2000 (n = 154) and 2018 (n = 489). COPD includes overlap syndrome. KYPH = kyphoscoliosis; NMD = neuromuscular disorders; OHS = obesity hypoventilation syndrome; RLD = restrictive lung disorder; SRBD = sleep-related breathing disorders.*

Functional Tests, Nocturnal Pulse Oximetry, and Nocturnal Capnography

Results of spirometry, ABGs, nocturnal pulse oximetry, and nocturnal capnography are shown in Table 3. Distribution of values of daytime $Paco_2$ is shown in e-Figure 2. ABGs reported were performed without NIV. Most patients were normocapnic. However, daytime $Paco_2$ was ≥ 6 kPa in 170 patients (46%), ≥ 6.5 kPa in 99 patients (27%), and ≥ 7 kPa in 63 subjects (17%).

Mean nocturnal pulse oximeter oxygen saturation was ≥ 90% in 279 patients (80% of the 350 tracings available).

Ventilators

Devices used are listed in e-Table 3. Devices were mostly bilevel positive pressure devices (n = 478, 98%). Eleven patients (2%) had multimodal ventilators. Use of humidifiers and oxygen supplementation is reported in Table 4.

Modes and Settings

Most patients (n = 407; 86%) used a bilevel positive pressure device in a spontaneous/timed mode (ie, with fixed levels of positive end-expiratory pressure and pressure support and a backup respiratory rate). In this mode, the patient triggers the ventilator, and controlled cycles are provided only when the patients' respiratory rate drops under the preset backup respiratory rate (Fig 3A). None of the subjects included used a spontaneous or controlled mode. Volume-targeted (n = 49, 12%; iVAPS [ResMed]; AVAPS-AE [Philips Respironics]) and other autotitrating modes (n = 19, 5%) were used infrequently. Multimodal ventilators (n = 11, 2%) were used in either volume assist-control, pressure control, or pressure support modes, exclusively in restrictive disorders (NMDs, KYPH, and other restrictive disorders) (Table 5, e-Table 6).

Patients with OHS and overlap syndrome had the highest values for IPAP and EPAP. Details of the settings are provided in Table 4.

Interfaces

Facial masks were the most frequently used interfaces (n = 358, 73%), followed by nasal masks (n = 91, 19%) and nasal pillows (n = 40, 8%) (Fig 3B, Table 4).

TABLE 1] Characteristics of Patients Under Noninvasive Ventilation and Major Comorbidities

Characteristics	All Patients	COPD	Overlap Syndrome	Neuromuscular Disorders	OHS	Kyphoscoliosis	Other Restrictive Disorders	SRBD
No. (%)	489 (100)	135 (28)	55 (11)	79 (16)	127 (26)	29 (6)	22 (4)	42 (9)
Age, y	71 (59-77)	72 (67-78)	71 (65-81)	59 (41-73)	69 (59-77)	69 (53-79)	73 (64-78)	65 (51-74)
Sex, male	272 (56)	68 (50)	36 (65)	45 (57)	60 (47)	12 (41)	14 (64)	37 (88)
BMI, kg/m^2	31 (24-39)	28 (21-33)	32 (28-40)	24 (19-28)	41 (37-47)[a]	25 (19-32)	24 (19-29)	30 (27-35)
Time under NIV, mo	39 (14-73)	23 (9-48)	43 (19-73)	40 (12-105)	44 (20-78)	60 (26-133)	65 (35-109)	39 (9-91)
Comorbidities								
Systemic hypertension	334 (68)	91 (67)	46 (84)	31 (39)	104 (82)	18 (64)[a]	16 (73)	28 (67)
Obesity	271 (55)	52 (38)	38 (69)	16 (20)	127 (100)	11 (38)	4 (18)	22 (52)
Anxiety and/or depressive disorder	220 (45)	82 (17)	16 (29)	27 (34)	68 (53)	8 (28)	7 (32)	12 (29)
Dyslipidemia	209 (43)	56 (41)	28 (51)	16 (20)	73 (57)	12 (43)[a]	7 (32)	17 (40)
Type 2 diabetes	149 (30)	22 (16)	20 (36)	10 (13)	76 (60)	4 (14)[a]	6 (27)	11 (26)
Chronic heart failure	106 (22)	29 (21)	15 (27)	11 (14)	36 (28)	3 (11)[a]	7 (32)	5 (12)
Pulmonary hypertension	86 (18)	36 (27)	16 (29)	4 (5)	18 (14)	6 (21)[a]	5 (23)	1 (2)
Cerebrovascular disease	26 (5)	9 (7)	5 (9)	2 (2)	7 (5)	0 (0)[a]	1 (4)	2 (3)
Treatment with opiates	17 (3)	6 (4.4)	1 (2)	0 (0)	2 (2)	0 (0)	0 (0)	8 (19)

Values listed are the most recent values obtained. Values are expressed as median (interquartile range) or No. (%). NIV = noninvasive ventilation; OHS = obesity hypoventilation syndrome; SRBD = sleep-related breathing disorder.

[a]Missing data: n = 1.

TABLE 2] Specific Diagnoses for Patients With Neuromuscular Disorders, Restrictive Lung Disorders, and Sleep-Related Breathing Disorders

Specific Diagnoses	Value
Neuromuscular disorders	79
Myopathies	32 (40)
Congenital muscular dystrophies	14 (18)
Congenital myopathies	4 (5)
Myotonic muscular dystrophies	13 (16)
Amyotrophic lateral sclerosis	15 (19)
Phrenic nerve paralysis (unilateral and/or bilateral)	14 (18)
Brainstem or cervical cord injury	6 (8)
Spinal muscular atrophy type I or II	5 (6)
Demyelinating diseases (multiple sclerosis)	4 (5)
Myasthenia gravis	3 (4)
Missing data	1
Other restrictive disorders	22
Postpolio syndrome	9 (41)
Sequelae of thoracic surgery	5 (23)
End-stage pulmonary fibrosis	5 (23)
Bronchiectasis	2 (9)
Sleep-related breathing disorders	42
OSA syndrome	18 (43)
Emergent central sleep apnea syndrome	14 (33)
Central sleep apnea syndrome	10 (24)

Values expressed as No. (% of diagnostic category) or No.

Interestingly, IPAP of up to 25 cm H_2O (median, 18; IQR, 16-21) and EPAP up to 14 cm H_2O (median, 7; IQR, 5-10) were tolerated with nasal pillows, without excessive leaks. There was no association between choice of interface and leaks or AHI reported by ventilator software (AHI; mean ± SD; facial masks: 3.6 ± 5.5/h; nasal masks: 3.9 ± 5.4/h; nasal pillows: 4.8 ± 7.3/h, P = .33) (e-Figs 3A, 3B).

Other Adjuncts to NIV: Oxygen, Humidifier, and Use of Mechanical Insufflation/Exsufflation Device

All indications combined, 40% of patients received oxygen supplementation and 350 (72%) had a humidifier. Supplemental oxygen was most frequently prescribed in COPD (76%). Twenty patients used a mechanical insufflation/exsufflation device (NMD: n = 16, severe COPD: n = 3, KYPH: n = 1).

Daily Use of Ventilator

Average daily use of NIV was high in all diagnostic groups (missing values: n = 30) (Fig 4, Table 5). Only 35 subjects (8%, 454 values recorded) used their device < 3.5 h/d. By multivariable analysis (e-Table 7), we found no association between time spent on ventilator and prior use of CPAP, implementation as outpatient vs inpatient, choice of interface, major comorbidities, or age. Time spent on NIV was lower in patients with OHS and SRDB, and in subjects treated chronically with opioids. Conversely, time spent on ventilator increased with duration of treatment.

e-Figure 3B shows average daily use of NIV according to interface used: 430 ± 193 min with facial masks, 488 ± 256 min with nasal masks, and 439 ± 192 min with nasal pillows (P = .264).

Comments on Specific Groups

COPD (Including Patients With Overlap Syndrome, n = 190): BMI: Fourteen patients (7%) had a BMI ≤ 18 kg/m^2. Conversely, 90 (47%) were obese. Twenty-nine percent had concomitant OSAS. Follow-up $Paco_2$ without NIV (n = 169) was ≤ 6 kPa in 76 subjects (45%), ≤ 6.5 kPa in 108 subjects (64%), and ≥ 8 kPa in 12 subjects (7%) (21 missing values).

Patients With OHS (n = 127): $Paco_2$ (39 missing values): $Paco_2$ without NIV (n = 88) was ≤ 6 kPa in 60 subjects (68%), ≤ 6.5 kPa in 76 subjects (86%), and ≥ 8 kPa in one subject.

Very Dependent Patients (Use of NIV > 16 h/d): Ten patients (median age, 63 years; IQR, 36-70; 60% men; median BMI, 19 kg/m^2; IQR, 16-24) used their ventilator > 16 h/d (median, 1'222 min; IQR, 1'093-1'309): seven had NMD (amyotrophic lateral sclerosis and Duchenne muscular dystrophy), two had COPD, and one had KYPH.

Implementation and Follow-up

NIV was initiated electively in 247 subjects (50%) vs in an emergency setting for 220 (45% of all patients; not specified for 22 patients; 5%). Most patients were started on NIV as inpatients (n = 400; 82%) vs 73 (15%) as outpatients (not specified for 16 patients; 3%). Initiating NIV in an outpatient setting was more frequent in subjects with SRBDs (45% of total), OHS (21%), and NMDs (17%).

One-third (n = 174; 36%) of all patients were followed exclusively by a pulmonologist in private practice. All other subjects were followed either by one of the four hospitals participating in this study (n = 243; 49%), or cooperatively by a pulmonologist and a hospital center (n = 72; 15%). Most patients were followed at least on a

TABLE 3] Spirometry, Arterial Blood Gases (Without Ventilator), Nocturnal Pulse Oximetry, and Nocturnal Capnography Under Ventilator

	All Patients	COPD	Overlap Syndrome	Neuromuscular Disorders	OHS	Kyphoscoliosis	Other Restrictive Disorders	SRBD
No. (%)	489 (100)	135 (28)	55 (11)	79 (16)	127 (26)	29 (6)	22 (4)	42 (9)
Spirometry (n = 353; missing: 136)								
FEV_1 (% predicted)	46 (31-64)	30 (22-46)	46 (34-60)	45 (34-58)	66 (52-82)	39 (29-53)	34 (30-44)	93 (86-102)
FVC (% predicted)	62 (45-76)	64 (49-73)	69 (61-77)	44 (33-58)	69 (53-81)	41 (30-54)	34 (30-45)	94 (87-101)
FEV_1/FVC (% predicted)	83 (63-98)	54 (41-75)	76 (56-84)	98 (82-111)	97 (93-102)	92 (83-114)	99 (77-108)	102 (92-106)
Arterial blood gases (n = 372; missing: 117)								
pH	7.40 (7.38-7.43)	7.39 (7.38-7.42)	7.40 (7.38-7.43)	7.41 (7.39-7.44)	7.41 (7.39-7.43)	7.39 (7.37-7.42)	7.41 (7.39-7.43)	7.42 (7.39-7.44)
$Paco_2$, kPa	5.8 (5.3-6.5)	6.3 (5.7-7.1)	5.8 (5.2-6.4)	5.6 (5-6.1)	5.7 (5.3-6.3)	6 (5.3-7)	6.2 (5.5-7.1)	5.2 (4.7-5.4)
Pao_2,[a] kPa	9 (8-9.9)	8 (6.9-8.9)	8.8 (7.9-9.4)	9.8 (8.3-11)	9 (8.4-9.7)	8.7 (8.1-9.8)	9.3 (8.9-10.3)	10.6 (9.8-10.9)
HCO_3^-, mmol/L	26.9 (24.8-30)	28.8 (26.1-31.3)	27.4 (24.7-29.3)	26 (23.7-28.5)	26.4 (24.8-28.6)	26.9 (25-31)	28.8 (25.9-32.1)	24.9 (24.3-25.5)
Sao_2,[a] %	93.6 (91.3-95.6)	92 (89.4-94.1)	93.2 (90.3-94.4)	95.4 (92.6-96.3)	93.5 (92-95)	93.4 (90.9-96)	93.4 (93-97.2)	96 (95-96.8)
Nocturnal pulse oximetry (n = 350; missing: 139)								
Mean Spo_2, %	92.6 (90.2-94)	92.3 (90-94)	91.4 (88.9-93)	93.2 (91-95.3)	91.6 (89.3-93.4)	94 (92.3-95.5)	94 (92.4-94.7)	94.3 (92.3-95.2)
ODI ≥ 3%, events/h	7.3 (3.2-13.8)	6.8 (2.9-11)	7.4 (4.2-12.1)	5.6 (2-11.2)	9.9 (5.8-16)	7.5 (3.7-16.8)	4.4 (1.7-15)	6.9 (3.7-18.7)
Nocturnal capnography (n = 153; missing: 336)								
Mean $Ptcco_2$, kPa	6.2 (5.6-6.8)	6.4 (5.6-6.9)	6.2 (5.8-6.8)	5.7 (5.2-6.7)	6.1 (5.5-6.7)	5.9 (5.5-6.6)	6 (5.7-6.8)	6 (5.8-6.2)

ODI = oxygen desaturation index. See Table 1 legend for expansion of other abbreviations.
[a]Pao_2 and Sao_2 are room air values (Pao_2: n = 283; Sao_2: n = 275).

TABLE 4] Ventilator Modes, Interfaces, and Other Adjuncts to NIV

Modes, Interfaces and Adjuncts	All Patients	COPD	Overlap Syndrome	Neuromuscular Disorders	OHS	Kyphoscoliosis	Other Restrictive Disorders	SRBD
No. (%)	489 (100)	135 (28)	55 (11)	79 (16)	127 (26)	29 (6)	22 (4)	42 (9)
Bilevel ventilator modes	479 (98)[a]	135 (100)	55 (100)	71 (90)	127 (100)	28 (96.5)	20 (91)	42 (100)
Spontaneous/timed mode	407 (83)	115 (86)	46 (84)	63 (80)	107 (84)	27 (93)	20 (91)	29 (71)
iVAPS mode	29 (6)	12 (9)	4 (7)	4 (6)	8 (6)	1 (3.5)	…	…
AVAPS-AE mode	20 (4)	5 (4)	3 (5)	2 (2)	10 (8)	…	…	…
Other modes	19 (4)	2 (1)	2 (4)	1 (1)	2 (2)	…	…	12 (29)
Multimodal ventilator modes	11 (2)[b]	…	…	8 (10)[b]	…	1 (3.5)	2 (9)	…
VAC mode	5 (1)	…	…	2 (3)	…	1 (3.5)	2 (9)	…
PC mode	4 (0.8)	…	…	4 (6)	…	…	…	…
PS mode	1 (0.2)	…	…	1 (1)	…	…	…	…
Interfaces								
Facial mask	359 (73)	115 (85)	45 (82)	44 (56)	96 (76)	15 (52)	16 (73)	28 (67)
Nasal mask	91 (19)	12 (9)	7 (13)	22 (28)	27 (21)	11 (38)	4 (18)	8 (19)
Nasal pillows	40 (8)	8 (6)	3 (5)	15 (19)	3 (2)	3 (10)	2 (9)	6 (14)
Other adjuncts to NIV								
Oxygen	196 (40)	103 (76)	22 (40)	7 (9)	40 (31)	11 (38)	11 (50)	2 (5)
Humidifier	350 (72)	107 (79)	43 (78)	58 (73)[c]	86 (68)	20 (69)	13 (59)	24 (57)

Values listed are the most recent values obtained. Values are expressed as No. (%). AVAPS-AE = average volume assured pressure support-automatic expiratory positive airway pressure; iVAPS = intelligent volume-assured pressure support; Other modes = autospontaneous/timed, VAuto, or spontaneous modes; PC = pressure control ventilation; PS = pressure support ventilation; VAC = volume assist-control ventilation. See Table 1 legend for expansion of other abbreviations.
[a]Missing data: n = 3.
[b]Missing data: n = 1.
[c]Missing data: n = 2.

yearly basis: 88% (n = 431) had been evaluated within the preceding 12 months.

When compared with hospital-based follow-ups, patients followed by pulmonologists in private practice had their treatment initiated more often as outpatients (27% vs 9%) and were more often on bilevel positive pressure devices in spontaneous/timed mode (91% vs 80%). Pulmonologists in private practice tended to follow a higher percentage of patients with OHS (55 of 174, 32% vs 72 of 315, 23%) and SRBD (22 of 174, 13% vs 20 of 315, 6%), whereas patients with NMD were managed more frequently by hospitals (59 of 315, 19% vs 20 of 174, 11%). Number of comorbidities, average daily use of ventilator, and correction of SRDBs did not differ significantly between subjects with a hospital-based or a liberal pulmonologist-based follow-up.

Discussion

This study is to our knowledge the largest detailed descriptive report of an unselected population of subjects treated by long-term NIV. Patients were on average in their 70s, with a slight male preponderance; most were obese and had several comorbidities. They were almost exclusively ventilated with bilevel pressure support ventilators in spontaneous/timed mode, and used their ventilator approximately 7 h/d. Most patients had their treatment initiated in a hospital setting (82%), with only one-half in an emergency situation. Adherence to treatment was on average excellent, with 8% of

TABLE 5] Ventilator Settings According to Modes

Settings, AHI, and Compliance	All Patients	COPD	Overlap Syndrome	NMD	OHS	Kyphoscoliosis	Other RLDs	SRBD
No. (%)	489 (100)	135 (28)	55 (11)	79 (16)	127 (26)	29 (6)	22 (4)	42 (9)
Bilevel ventilators, ST mode (n = 407)								
IPAP, cm H_2O[a]	18 (16-21)	18 (16-20)	20 (18-22)	15 (13-18)	21 (18-24)	17 (16-20)	18 (16-20)	17 (15-18)
EPAP, cm H_2O[a]	7 (5-10)	6 (5-7)	8 (7-10)	5 (4-7)	10 (7-11)	6 (5-8)	6 (5-7)	10 (7-12)
BURR, cycles/min[b]	14 (12-17)	14 (12-16)	16 (14-18)	14 (12-16)	14 (12-18)	14 (14-16)	15 (13-17)	14 (12-16)
Bilevel ventilators, volume-targeted modes (n = 49)								
ResMed devices	29 (6)	12 (9)	4 (7)[c]	4 (5)[c]	8 (6)	1 (3)[c]	0 (0)	0 (0)
Targeted VA, L/min[d]	5.2 (5.2-5.2)	5.2 (5.2-5.2)	…	…	5.2 (5.2-5.5)	…	…	…
Targeted RR, cycles/min[a]	15 (13-15)	15 (13.5-15)	…	…	14 (13-15)	…	…	…
Philips Respironics devices	20 (4)	5 (4)	3 (5)[c]	2 (2)[c]	10 (13)	0 (0)	0 (0)	0 (0)
Targeted V_T, mL	500 (500-555)	570 (550-600)	…	…	500 (500-500)	…	…	…
Targeted V_T/body weight, mL/kg	5 (4.5-5.9)	5.1 (5-6)	…	…	4.7 (4.2-5)	…	…	…
Bilevel positive pressure ventilators, ResMed (n = 381; 78% of total) and Lowenstein Medical devices (n = 11, 2% of total)								
AHI, No./h	1.5 (0.4-4.1)	1 (0.3-3)	2.1 (1.2-5)	1.8 (0.5-4.6)	1.3 (0.3-3.1)	2.2 (0.1-4.7)	0.8 (0.2-1.8)	4.9 (1.6-9.4)
Mean daily use, min/d	428 (310-532)	448 (333-549)	428 (376-531)	485 (293-600)	378 (255-496)	414 (310-518)	511 (446-672)	368 (298-454)
Bilevel positive pressure ventilators, Philips Respironics devices (n = 87; 18% of total)								
AHI, No./h	3.4 (1.8-9.1)	3.3 (1.5-3.9)	2.6 (1.7-3.3)	3.8 (3-7.9)	6.7 (1.8-10)	3.5 (2.6-7.1)	1.9 (1.8-2.4)	9.3 (8.5-10.6)
Mean daily use, min/d	425 (336-542)	464 (370-567)	503 (377-584)	415 (347-488)	422 (326-534)	491 (428-519)	579 (473-595)	322 (287-347)

Values listed are the most recent values obtained. Values are expressed as median (interquartile range) or No. (%). See e-Tables 4, 5 for further details and data provided by ventilator software. Results are presented separately according to manufacturer of device because settings, software, and data presentation differ. AHI = apnea-hypopnea index; BURR = backup respiratory rate; EPAP = expiratory positive airway pressure; IPAP = inspiratory positive airway pressure; NMD = neuromuscular disease; RR = respiratory rate; ST = spontaneous/timed; VA = alveolar volume; V_T = tidal volume.

[a]Missing data: n = 2.

[b]Missing data: n = 3.

[c]Values are not reported because of a limited number of patients.

[d]Missing data: n = 1.

patients (n = 35) only using their device < 3.5 h. Patient follow-up was either hospital-based or performed by a private practitioner (pulmonologist) with minor differences between populations followed and no significant difference in terms of end points, such as AHI or average daily use of NIV.

Prevalence of NIV in our area (presently 37.9 per 100,000 inhabitants) has increased 2.5-fold over the last 18 years.[3] These figures are similar to those reported by European countries with a national registry: 47 per 100,000 inhabitants in Norway (2019, Norwegian National registry for long-term ventilation), 33 per 100,000 inhabitants in Sweden (2018 report, Swedevox), and 39.5 per 100,000 inhabitants in Finland (2018).[22] To put these results in perspective, the Eurovent study, a survey performed in 2001 to 2002 covering 16 European countries and 27,118 users, estimated prevalence of NIV to be 6.6 per 100,000 inhabitants.[23]

COPD (n = 190, including overlap syndrome) is now by far the most important group of patients treated by home NIV in this area: they represent 39% of all patients included (as opposed to 27.5% in 2000). They are in their early 70s (Table 1), with no sex predominance, comorbid, most often overweight (n = 35; 18%) or obese (n = 90; 47%), and have severe or very severe airway obstruction. Twenty-nine percent had concomitant OSAS (overlap syndrome). They have the same phenotype as those described as being the most frequent cause of noniatrogenic acute hypercapnic respiratory failure leading to invasive or noninvasive ventilation in the ICU.[24] Almost all patients were on bilevel positive pressure ventilators in a spontaneous/timed mode (n = 161; 85%), and only 24 (13%) used volume-targeted modes. Two-thirds (n = 125; 66%) had supplemental oxygen. Interestingly, average inspiratory pressures (IPAP: 18.7 ± 4 cm H_2O) were slightly lower than in the multicentric German randomized controlled trial by Kohnlein et al[25] (IPAP: 21.6 ± 4.7 cm H_2O). In spite of this, median values for daytime $Paco_2$ were within the targets set by Kohnlein et al[25] and average compliance was actually higher (7.6 ± 3.0 vs 5.9 ± 3.0 h) in the present study. Comparisons are however merely indicative: this was not a prospective cohort, but a group of patients treated by NIV for a median of 39 months (IQR, 14-73), with a possible selection of the more compliant subjects overtime.

OHS was the second group of importance and included 26% of all patients (n = 127) on NIV. They were in their

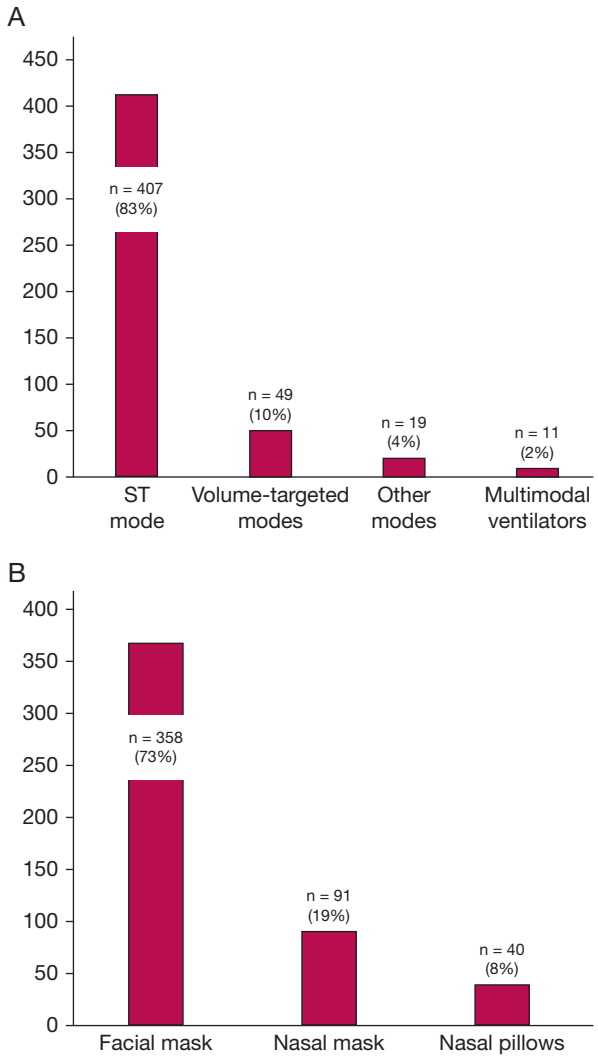

Figure 3 – *A, Distribution of ventilator modes used by the 489 patients studied. See e-Table 3 for details. B, Distribution of interfaces used by the 489 patients studied. ST = spontaneous/timed.*

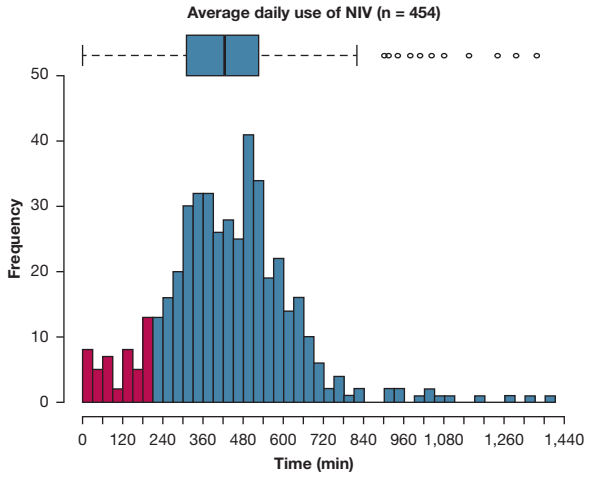

Figure 4 – *Distribution of average daily use of ventilator in 454 patients with data available from ventilator software. See Figure 1 legend for expansion of abbreviation.*

late 60s (Table 1), with a slight male predominance, and a high rate of metabolic syndromes (n = 53; 42%). Most patients were on bilevel positive pressure ventilators in a spontaneous/timed mode (n = 107; 84%), and only 18 (14%) used volume-targeted modes. Pressure settings were similar to those reported in the Pickwick study; however, in this multicentric Spanish study, a volume-targeted mode was used.[26] Median compliance was > 6 h/d (6.3 ± 2.7 h), with only 13 patients (10%) using their device < 3.5 h/d. Residual AHI (according to device software) was normalized in most cases.

The medical literature shows that CPAP can be as efficient as NIV in OHS, even in the presence of severe hypercapnia,[27-29] and guidelines have only been updated recently.[30] The data in our study do not allow to determine if there is already in our area a substantial proportion of patients with OHS who are treated initially by CPAP. Our impression is that this will be an important change in the near future.

Interfaces and AHI

A high proportion of patients (73%) used facial masks. This proportion reached 85% in COPD.[31] Although physicians are increasingly aware of the impact of facial masks on upper airway resistance under CPAP or NIV,[32] studies report a high use of facial masks in chronic NIV. For instance, a survey by Callegari et al[31] reported a 77% use of facial masks in a real-life study of long-term NIV in COPD. In that report, use of facial masks increased when NIV had been initiated after an acute exacerbation, with higher IPAP and lower BMI. Some authors suggest that, historically, especially in COPD, nasal masks were the default option in older studies because of lower insufflation pressures.[33] Several other groups have reported a more frequent use of facial vs nasal masks or even a default use of facial masks in long-term NIV.[34-36] Full face masks were also the default option in the Pickwick study of NIV in OHS.[37]

AHI reported by ventilator software was low for all diagnostic categories, without any significant difference according to interface used. Use of AHI as a surrogate measurement for polygraphic or polysomnographic assessment is debated, but three independent studies have shown a satisfactory agreement between AHI obtained with ventilator software and PSG assessment.[38-40] Choice of interface was not associated with significant differences in average daily use of ventilator or residual AHI reported by ventilator software.

Modes

Autotitrating modes were seldom used in this observational study (16%). Interestingly, although a plug and play type of option may seem more appealing to pulmonologists in private practice, this option was used in fact more often in one hospital center, irrespective of the underlying diagnosis. These modes have not yet convinced ventilator prescribers in this area: indeed, the available data suggest that they do at most as well as usual settings.[6,7,9-14,41-43] Volume-cycled ventilators and volume assist-control modes have virtually disappeared, confirming the trend previously described.[3]

Initiation and Follow-up

Most new NIV treatments were initiated as in-patients. For 45% of the population, NIV was started after an acute episode of hypercapnic respiratory failure. There is a trend in favor of increasing implementation of NIV on an outpatient basis, especially in SRBDs, OHS, and NMDs. The limitations are mainly related to availability of beds in day care structures with trained health-care workers.

It is a specificity of Switzerland that pulmonologists in private practice can prescribe, initiate, and follow patients with chronic hypercapnic respiratory failure put on NIV, alone or with a health-care provider. For patients followed by pulmonologists in private practice, NIV had been more frequently initiated on an outpatient basis; there were minor differences as to choice of modes, but no significant differences as to diagnoses, comorbidities, number of patients seen within the preceding 12 months, or end points such as AHI or average daily use of NIV.

Modalities of follow-up were in agreement with the SomnoNIV[16] recommendations, and polygraphy or polysomnography are not routine procedures in this population. Routine monitoring includes the following: (1) targeted clinical assessment, (2) ABGs, (3) nocturnal pulse oximetry, and (4) synthesis report from ventilator software. Nocturnal capnography is limited for outpatients in Switzerland because there is no consensus on reimbursement for home nocturnal capnography.

Study Limitations

There are several limitations to this study. First, it is a purely observational study; therefore, data presented cannot be used to validate or support the indication or efficacy of NIV in any of the patient groups we analyzed. However, the large number of unselected subjects, and

the fact that most patients have spent several years under NIV, with a good adherence to their treatment, supports the modes and settings of NIV, which are described. Second, there are missing values in follow-up tests: these result from the real-life design of this study, and allow to appreciate how these patients are followed in an area which is familiar with the use of NIV since the mid-1980s. Third, data reported concerning AHI and average daily use of NIV must be considered as describing a selection of patients who have pursued and accepted their treatment for at least 3 months, and most often for several years: this is not a cohort study, and noncompliant or less compliant subjects who may have interrupted their treatment before 3 months are not reported. Fourth, these observations may not be representative of other regions of the world where demographics (BMI, ethnicity, and socioeconomic status) differ. Finally, choice of devices, settings, interfaces, oxygen supplementation, and follow-up tests performed relied entirely on the attending physician(s).

Conclusions

In this large observational study of home NIV, COPD is presently the most important group of patients, followed by those with OHS. Prevalence of NIV has increased 2.5-fold since 2000. Patients are on average in their 70s, with frequent comorbidities; more than one-half are obese, and approximately 30% are > 75 years of age. Devices used are almost exclusively pressure-cycled, with a low use of volume-targeted and autotitrating modes. Results in terms of control of $Paco_2$, AHI, and average daily use were similar to those published in the randomized controlled trials concerning COPD and OHS.

Acknowledgments

Author contributions: All authors have approved the version to be published and agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. All authors have provided substantial contributions to the conception or design of the work, or the acquisition, analysis, or interpretation of data for the work and to drafting the work or revising it critically for important intellectual content.

Financial/nonfinancial disclosures: None declared.

Role of sponsors: The sponsor had no role in the design of the study, the collection and analysis of the data, or the preparation of the manuscript.

Other contributions: We thank the Ligue Pulmonaire Genevoise (www.lpge.ch) for its financial support. We also thank the pulmonologists in private practice who accepted to participate in this study and made available their medical files. We also thank all the health-care providers and device manufacturers in our area for their help in obtaining a complete database of patients under home mechanical ventilation in the Cantons of Geneva and Vaud: The Pulmonary leagues (Ligue Pulmonaire Genevoise and Ligue Pulmonaire Vaudoise), ResMed Schweiz, Philips Respironics, the CENAS sleep centre, SOS Oxygène Suisse SA, and Sleep & Health. We also thank Antoine Poncet, MS, for his expertise and help in computing the statistics of this study.

Additional information: The e-Figures and e-Tables can be found in the Supplemental Materials section of the online article.

References

1. Sullivan CE, Issa FG, Berthon-Jones M, Eves L. Reversal of obstructive sleep apnoea by continuous positive airway pressure applied through the nares. *Lancet*. 1981;1(8225):862-865.
2. King AC. Long-term home mechanical ventilation in the United States. *Respir Care*. 2012;57(6):921-930.
3. Janssens JP, Derivaz S, Breitenstein E, et al. Changing patterns in long-term noninvasive ventilation: a 7-year prospective study in the Geneva Lake area. *Chest*. 2003;123(1):67-79.
4. Sanders MH, Kern N. Obstructive sleep apnea treated by independently adjusted inspiratory and expiratory positive airway pressures via nasal mask. Physiologic and clinical implications. *Chest*. 1990;98(2):317-324.
5. Strumpf DA, Millman RP, Hill NS. The management of chronic hypoventilation. *Chest*. 1990;98(2):474-480.
6. Windisch W, Storre JH. Target volume settings for home mechanical ventilation: Great progress or just a gadget? *Thorax*. 2012;67(8):663-665.
7. Arellano-Maric MP, Gregoretti C, Duiverman M, Windisch W. Long-term volume-targeted pressure-controlled ventilation: Sense or nonsense? *Eur Respir J*. 2017;49(6).
8. Piper AJ. Advances in non-invasive positive airway pressure technology. *Respirology*. 2020;25(4):372-382.
9. Nilius G, Katamadze N, Domanski U, Schroeder M, Franke KJ. Non-invasive ventilation with intelligent volume-assured pressure support versus pressure-controlled ventilation: effects on the respiratory event rate and sleep quality in COPD with chronic hypercapnia. *Int J Chron Obstruct Pulmon Dis*. 2017;12:1039-1045.
10. McArdle N, Rea C, King S, et al. Treating chronic hypoventilation with automatic adjustable versus fixed EPAP Intelligent Volume-Assured Positive Airway Pressure Support (iVAPS): a randomized controlled trial. *Sleep*. 2017;40(10).
11. Murphy PB, Davidson C, Hind MD, et al. Volume targeted versus pressure support non-invasive ventilation in patients with super obesity and chronic respiratory failure: a randomised controlled trial. *Thorax*. 2012;67(8):727-734.
12. Murphy PB, Arbane G, Ramsay M, et al. Safety and efficacy of auto-titrating noninvasive ventilation in COPD and obstructive sleep apnoea overlap syndrome. *Eur Respir J*. 2015;46(2):548-551.
13. Kelly JL, Jaye J, Pickersgill RE, Chatwin M, Morrell MJ, Simonds AK. Randomized trial of 'intelligent' autotitrating ventilation versus standard pressure support non-invasive ventilation: impact on adherence and physiological outcomes. *Respirology*. 2014;19(4):596-603.
14. Jaye J, Chatwin M, Dayer M, Morrell MJ, Simonds AK. Autotitrating versus standard noninvasive ventilation: a randomised crossover trial. *Eur Respir J*. 2009;33(3):566-571.
15. 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.
16. Janssens JP, Borel JC, Pepin JL, SomnoNIVG. Nocturnal monitoring of home non-invasive ventilation: the contribution of simple tools such as pulse oximetry, capnography, built-in ventilator software and autonomic markers of sleep fragmentation. *Thorax*. 2011;66(5):438-445.

17. Pasquina P, Adler D, Farr P, Bourqui P, Bridevaux PO, Janssens JP. What does built-in software of home ventilators tell us? An observational study of 150 patients on home ventilation. *Respiration*. 2012;83(4):293-299.

18. Leger P, Bedicam JM, Cornette A, et al. Nasal intermittent positive pressure ventilation. Long-term follow-up in patients with severe chronic respiratory insufficiency. *Chest*. 1994;105(1):100-105.

19. Simonds AK, Elliott MW. Outcome of domiciliary nasal intermittent positive pressure ventilation in restrictive and obstructive disorders. *Thorax*. 1995;50(6):604-609.

20. Goldberg A. Clinical indications for noninvasive positive pressure ventilation in chronic respiratory failure due to restrictive lung disease, COPD, and nocturnal hypoventilation—a consensus conference report. *Chest*. 1999;116(2):521-534.

21. Piper AJ, Grunstein RR. Obesity hypoventilation syndrome: mechanisms and management. *Am J Respir Crit Care Med*. 2011;183(3):292-298.

22. Kotanen P, Hanna-Riikka K, Kainu A, Brander P, editors. The prevalence of chronic respiratory failure treated with home mechanical ventilation in Helsinki, Finland. European Respiratory Society Congress; September 30, 2019; Madrid, Spain.

23. 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.

24. Adler D, Pepin JL, Dupuis-Lozeron E, et al. Comorbidities and subgroups of patients surviving severe acute hypercapnic respiratory failure in the intensive care unit. *Am J Respir Crit Care Med*. 2017;196(2):200-207.

25. 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.

26. Masa JF, Corral J, Caballero C, et al. Non-invasive ventilation in obesity hypoventilation syndrome without severe obstructive sleep apnoea. *Thorax*. 2016;71(10):899-906.

27. Howard ME, Piper AJ, Stevens B, et al. A randomised controlled trial of CPAP versus non-invasive ventilation for initial treatment of obesity hypoventilation syndrome. *Thorax*. 2017;72(5):437-444.

28. Masa JF, Mokhlesi B, Benitez I, et al. Long-term clinical effectiveness of continuous positive airway pressure therapy versus non-invasive ventilation therapy in patients with obesity hypoventilation syndrome: a multicentre, open-label, randomised controlled trial. *Lancet*. 2019;393(10182):1721-1732.

29. Soghier I, Brozek JL, Afshar M, et al. Noninvasive ventilation versus CPAP as initial treatment of obesity hypoventilation syndrome. *Ann Am Thorac Soc*. 2019;16(10):1295-1303.

30. Mokhlesi B, Masa JF, Brozek JL, et al. Evaluation and management of obesity hypoventilation syndrome. An Official American Thoracic Society Clinical Practice Guideline. *Am J Respir Crit Care Med*. 2019;200(3):e6-e24.

31. Callegari J, Magnet FS, Taubner S, et al. Interfaces and ventilator settings for long-term noninvasive ventilation in COPD patients. *Int J Chron Obstruct Pulmon Dis*. 2017;12:1883-1889.

32. Schellhas V, Glatz C, Beecken I, et al. Upper airway obstruction induced by non-invasive ventilation using an oronasal interface. *Sleep Breath*. 2018;22(3):781-788.

33. Storre JH, Callegari J, Magnet FS, et al. Home noninvasive ventilatory support for patients with chronic obstructive pulmonary disease: patient selection and perspectives. *Int J Chron Obstruct Pulmon Dis*. 2018;13:753-760.

34. Crimi C, Noto A, Princi P, et al. Domiciliary non-invasive ventilation in COPD: an international survey of indications and practices. *COPD*. 2016;13(4):483-490.

35. 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.

36. 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.

37. Masa JF, Corral J, Alonso ML, et al. Efficacy of different treatment alternatives for obesity hypoventilation syndrome. Pickwick study. *Am J Respir Crit Care Med*. 2015;192(1):86-95.

38. Georges M, Adler D, Contal O, et al. Reliability of apnea-hypopnea index measured by a home bi-level pressure support ventilator versus a polysomnographic assessment. *Respir Care*. 2015;60(7):1051-1056.

39. Fernandez Alvarez R, Rabec C, Rubinos Cuadrado G, et al. Monitoring noninvasive ventilation in patients with obesity hypoventilation syndrome: comparison between ventilator built-in software and respiratory polygraphy. *Respiration*. 2017;93(3):162-169.

40. Sogo A, Montanya J, Monso E, Blanch L, Pomares X, Lujan M. Effect of dynamic random leaks on the monitoring accuracy of home mechanical ventilators: a bench study. *BMC Pulm Med*. 2013;13:75.

41. Janssens JP, Metzger M, Sforza E. Impact of volume targeting on efficacy of bi-level non-invasive ventilation and sleep in obesity-hypoventilation. *Respir Med*. 2009;103(2):165-172.

42. Storre JH, Seuthe B, Fiechter R, et al. Average volume-assured pressure support in obesity hypoventilation: a randomized crossover trial. *Chest*. 2006;130(3):815-821.

43. Ekkernkamp E, Storre JH, Windisch W, Dreher M. Impact of intelligent volume-assured pressure support on sleep quality in stable hypercapnic chronic obstructive pulmonary disease patients: a randomized, crossover study. *Respiration*. 2014;88(4):270-276.