Changing Patterns in Long-term Noninvasive Ventilation*

A 7-Year Prospective Study in the Geneva Lake Area

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Study objectives: **To describe a 7-year follow-up (1992 to 2000) of patients who were treated by home nasal positive-pressure ventilation (NPPV) for chronic hypercapnic respiratory failure.**
Design: **Prospective descriptive study.**
Setting: **Two university hospitals and a pulmonary rehabilitation center.**
Patients: **Two hundred eleven patients with obstructive pulmonary disorders (58 patients) or restrictive pulmonary disorders (post-tuberculosis, 23 patients; neuromuscular diseases [NM], 28 patients; post-poliomyelitis syndrome, 12 patients; kyphoscoliosis [KYPH], 19 patients; obesity-hypoventilation syndrome [OHS], 71 patients) who were treated by long-term NPPV.**
Intervention: **Annual, elective, standardized medical evaluations.**
Measurements: **Pulmonary function tests, arterial blood gas levels, health status, compliance, survival and probability of pursuing NPPV, and hospitalization rates.**
Results: **Patients with OHS, NM, and KYPH had the highest probability of pursuing NPPV, while patients with COPD had the lowest values. Overall, the compliance rate was high (noncompliance rate, 15%). As of 1994, COPD and OHS became the most frequent indications for NPPV, increasing regularly, while other indications remained stable. The use of pressure-cycled ventilators progressively replaced that of volume-cycled ventilators in most indications. Hospitalization rates decreased in all groups after initiating NPPV, when compared with the year before NPPV, for up to 2 years in COPD patients, and 5 years in non-COPD patients.**
Conclusion: **Major changes in patient selection for NPPV occurred during the study period with a marked increase in COPD and OHS. The shift toward less expensive pressure-cycled ventilators and the decrease in hospitalizations after initiating NPPV have had positive impacts on the cost-effectiveness of NPPV in patients with chronic respiratory failure.**
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Key words: COPD; intermittent positive-pressure ventilation; noninvasive positive-pressure ventilation; obesity-hypoventilation syndrome

Abbreviations: ABG = arterial blood gas; ANTADIR = National Association for Home Care of Patients with Chronic Respiratory Insufficiency; BMI = body-mass index; CPAP = continuous positive airway pressure; HAD = hospital anxiety and depression; HMV = home mechanical ventilation; KYPH = kyphoscoliosis; LTOT = long-term oxygen therapy; NM = neuromuscular; NPPV = nasal positive-pressure ventilation; OHS = obesity-hypoventilation syndrome; OSAS = obstructive sleep apnea syndrome; $P_{E}max$ = maximal mouth expiratory pressure; $P_{I}max$ = maximal mouth inspiratory pressure; POLIO = post-polio syndrome; PPV = positive-pressure ventilation; PRC = pulmonary rehabilitation center; QOL = quality of life; Sa_{O_2} = arterial oxygen saturation; TB = tuberculosis

Until the early 1980s, long-term positive-pressure ventilation (PPV) was delivered either invasively, by tracheostomy, or, although rarely in Western Europe, by mouth.[1] The first reports of nasal PPV (NPPV) were those of Rideau[2] and Delaubier et al,[3] who described the successful management of two patients with Duchenne muscular dystrophy by

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NPPV over a 2-year period. As of 1987, several groups had reported[4–9] on the successful use of NPPV in patients with chronic respiratory failure related to neuromuscular (NM) diseases, chest wall diseases, or post-poliomyelitis syndrome (POLIO). Thereafter, the increase in the number of patients treated by NPPV was spectacular. In France, the number of patients receiving NPPV treated by the National Association for Home Care of Patients With Chronic Respiratory Insufficiency (ANTADIR) increased from 130 in 1988, to 3,120 in 1998.[10] The first reports of NPPV in Switzerland were published in 1989.[11] At the end of 1989, nationwide, 46 patients were receiving home mechanical ventilation (HMV; 30% used NPPV). At present, 500 patients are receiving NPPV in Switzerland, with 155 being treated in the Geneva Lake area (*ie*, a prevalence of 15 per 10^5 inhabitants).[12]

Two major changes have occurred in HMV during the past 10 years. The first is that of patient selection, with a marked increase in long-term ventilation therapy for patients with COPD and obesity-hypoventilation syndrome (OHS).[13–16] The second change is that of the equipment used for home NPPV. Bilevel pressure-cycled ventilation, which was introduced in the early 1990s,[17,18] has been increasingly used over the past 8 years, mainly because of lower costs than volume-cycled ventilation, lighter weight of the equipment, in many cases improved patient comfort, and simplicity of use. Several retrospective reports[8,19–23] have shown the feasibility of long-term domiciliary NPPV in patients with restrictive and obstructive respiratory disorders. However, either all or most patients in these studies were treated with volume-cycled ventilators. No long-term data are yet available for patients treated with pressure-cycled ventilators. The present study describes the changes that occurred over a 7-year observation period (1992 to 2000) in a cohort of patients treated by home NPPV in the Geneva Lake area. We shall emphasize the changes in the equipment used for NPPV (with their impact on the correction of hypercapnia, the probability of pursuing NPPV, and survival) and the changes in patient selection. The impact of NPPV on the use of health resources (*ie*, hospitalizations) in restrictive or obstructive lung disorders also will be discussed.

Materials and Methods

As of October 1992, all patients treated by home NPPV in the cantons of Geneva and Vaud (1,030,000 inhabitants [year 2000 census]) were prospectively included in a computerized database. Patients with tracheostomies were not included in this analysis. In Switzerland, the use of tracheostomy for long-term PPV is very restrictive (at present, $< 5\%$ of patients receive HMV).

Patients were started on NPPV therapy either after an acute episode of hypercapnic respiratory failure or electively, due to the progression of alveolar hypoventilation. The decision to implement NPPV therapy for all patients included in this study was subjected to approval by a panel of experts from the Swiss Pulmonary League (a national association for the care of patients with respiratory diseases). In Switzerland, this expert opinion is a prerequisite for coverage by medical insurance. This group also provides recommendations about the choice of equipment and publishes regularly revisited guidelines concerning indications for home NPPV use.[24]

All patients underwent standardized yearly medical evaluations including pulmonary function tests, the measurement of arterial blood gas (ABG) levels, maximal inspiratory and expiratory mouth pressures, the measurement of dyspnea, and scoring for emotional disorders, physical autonomy, and compliance. Other tests that were performed routinely were not included in the database. Patient follow-up consisted of regular home visits by registered nurses and outpatient consultations at a frequency that varied according to the patient's clinical condition. The following four medical centers participated in the study: the Pulmonary Division of Geneva University Hospital; the Pulmonary Division of Lausanne University Hospital; a pulmonary rehabilitation center (PRC; Rolle, Vaud, Switzerland); and the Children's Hospital of Geneva University Hospital (four patients). The study protocol was accepted by the Ethics Committee of Geneva University Hospital.

Pulmonary Function Tests

Forced expiratory volumes (*ie*, FEV_1, FVC, and FEV_1/FVC ratio) were measured as recommended by the American Thoracic Society standards using either of two spirometers (Alpha spirometer; Vitalograph, Ltd; Buckingham, UK; or model 6200 Autobox; SensorMedics; Yorba Linda, CA).[25] Values are expressed as the percentage of predicted values.[26] Pulmonary muscle strength was determined by measuring maximal inspiratory pressure (PImax) and maximal expiratory pressure (PEmax) using a mouth pressure meter (Micro Medical Ltd; Gillingham, UK).[27] PImax was measured at residual volume, and PEmax was measured at total lung capacity. For each patient, three to six maneuvers were performed with the goal of having the two maneuvers with the highest values matching within 10%. The values reported are the best values obtained. ABG levels were measured by puncture of the radial artery (gas analyzer ABL 330; Radiometer; Copenhagen, Denmark) after at least 1 h without the patient receiving NPPV and after at least 1 h of receiving NPPV. When feasible, a 6-min walk test was performed in a corridor that was 50 m long, as described by McGavin et al.[28]

The monitoring of nocturnal ventilation was performed by pulse oximetry (Minolta Pulsox-7 pulse oximeter; AVL Medical Instruments SA; Schaffhausen, Switzerland; or Ohmeda Biox-IV; Laubscher AG; Hölstein, Switzerland). In one center (PRC, Rolle), continuous nocturnal monitoring of transcutaneous CO_2 was introduced in 1996 (TINA TCM3; Radiometer).[29]

In all three centers, the adjustment of ventilator settings and oxygen supplementation aimed to obtain the lowest possible value for daytime $PaCO_2$ (or nocturnal transcutaneous CO_2 pressure) with the ventilator, and a mean nocturnal arterial oxygen saturation (SaO_2) of $> 90\%$, with $< 20\%$ of the total recording time $< 90\%$ of SaO_2.

Scoring for Dyspnea, Health Status, and Emotional Disturbances

Resting dyspnea was estimated by the patient using a Borg scale (a vertical, linear 20-cm scale that is labeled from 0 to 10)

with corresponding verbal expressions of perceived intensity (with higher values indicating more severe dyspnea).[30] A Karnofsky scale was used to assess the degree of dependence in performing daily activities (range, 0 to 10). Patients who are capable of maintaining a regular professional or scholastic activity have scores between 8 and 10. Patients who are incapable of maintaining a regular professional activity, and need varying degrees of assistance in their daily activities, have scores between 5 and 7. Scores of < 4 describe patients with a severe handicap who need assistance equivalent to that dispensed by a hospital. The hospital anxiety and depression (HAD) questionnaire was used to screen for anxiety or depression. It contains 14 multiple-choice questions, with 7 questions oriented toward the detection of anxiety disorders and 7 questions oriented toward the detection of depression.[31,32]

Compliance With NPPV

Compliance was assessed regularly by the visiting nurses on the basis of the number of minutes of use that was recorded by built-in ventilator counters. Values were recorded several times per year and were averaged at 1-year intervals for study purposes. Interruptions of NPPV due to noncompliance were all recorded. *Noncompliance* was defined as an average yearly use of < 3.5 h per day.

Technical Aspects of NPPV

Ventilator type, all ventilator settings, the use of oxygen, and flow rates were recorded.

Hospitalization Rates Before and After Initiation of NPPV as Cost-effectiveness Indicators

For patients who live and are treated in the canton of Geneva, all hospitalizations are registered in a centralized database. The number of hospital stays and the number of days spent in a hospital per year before and after the initiation of NPPV therefore could be compared for 109 patients. This was not the case, however, for patients followed-up in the canton of Vaud (Pulmonary Division of Lausanne University Hospital and the PRC).

Statistical Analysis

The data are reported as the mean ± SD with range, unless specified otherwise. An unpaired *t* test or a Mann-Whitney rank sum test was used for the comparison of parametric or nonparametric (ordinal) data, respectively, between groups. A paired *t* test or a Wilcoxon signed rank test was used to compare parametric or nonparametric data, respectively, in patients receiving or not receiving ventilation, or in data collected in the same patients over time. Repeated-measures analysis of variance (for parametric data) or a Friedman test (for nonparametric data) was used to analyze repeated measurements in the same individuals over the duration of the study period. For the analysis of the use of NPPV and survival, we computed Kaplan-Meier curves. Comparisons between groups were performed using the a log rank test.[33] The level of significance for all tests was set at $p < 0.05$.

The database was recorded using appropriate software (Filemaker Pro 4.1 for PC computers; Filemaker Inc; Santa Clara, CA), and the statistical analysis was performed using a software package (Statview, version 5.0 for PC computers; Abacus Concepts; Piscataway, NJ).

Results

Patients

Between October 1, 1992 and February 1, 2000, 211 patients receiving home NPPV therapy were included in the study database. The length of follow-up ranged from 1 to 88 months (median, 24 months). Patients were divided into six diagnostic categories (Table 1).

The COPD group included 58 patients who had obstructive lung diseases and hypercapnic respiratory failure due to the following: emphysema and/or chronic bronchitis (51 patients); severe bronchiectasis (4 patients); or cystic fibrosis (3 patients). Four patients with severe hypercapnic COPD and two patients with cystic fibrosis used NPPV therapy as a bridge to transplantation and received ventilation for a mean duration of 8 ± 4 months (range, 3 to 14 months) before receiving a lung transplant. Systematic sleep studies were not routinely performed to exclude patients with overlap syndromes.

The OHS group included 71 patients, all of whom had experienced at least one episode of severe hypercapnic respiratory failure, were markedly obese (body mass index [BMI], 42 ± 9 kg/m^2) and had daytime hypercapnia even while receiving long-term treatment with NPPV (Table 2). Fifty patients (70%) had a presumptive diagnosis of associated obstructive sleep apnea syndrome (OSAS), which was based on clinical

Table 1—*Pulmonary Function Tests, Pressures, and BMI Values for 211 Patients Treated by NPPV

Variables	COPD (n = 58)	OHS (n = 71)	TB (n = 23)	NM (n = 28)	POLIO (n = 12)	KYPH (n = 19)
Age, yr	63 ± 13	64 ± 11	75 ± 6	47 ± 22	67 ± 11	60 ± 15
BMI, kg/m$_2$	25 ± 7	42 ± 10	22 ± 5	26 ± 8	21 ± 4	23 ± 6
FEV_1, % predicted	29 ± 14	61 ± 19	34 ± 14	42 ± 22	38 ± 12	32 ± 10
FVC, % predicted	56 ± 22	70 ± 18	40 ± 15	48 ± 28	44 ± 11	37 ± 12
FEV_1/FVC, % predicted	56 ± 18	90 ± 15	89 ± 18	96 ± 17	93 ± 23	95 ± 19
PImax, cm H_2O	52 ± 22	70 ± 24	39 ± 24	36 ± 13	37 ± 17	46 ± 23
PEmax, cm H_2O	71 ± 29	108 ± 42	55 ± 24	52 ± 28	61 ± 29	66 ± 23

*Values given as mean ± SD.

Table 2—*ABG Levels With and Without NPPV**

Variables	COPD (n = 58)	OHS (n = 71)	TB (n = 23)	NM (n = 28)	POLIO (n = 12)	KYPH (n = 19)
ABG levels without NPPV						
Pa_{O_2}	61 ± 13†	60 ± 12†	58 ± 11†	68 ± 11	62 ± 16‡	61 ± 9§
Pa_{CO_2}	53 ± 10‖	49 ± 10†	50 ± 6§	48 ± 8†	49 ± 10†	49 ± 6‡
pH	7.38 ± 0.04‡	7.38 ± 0.05†	7.4 ± 0.04§	7.4 ± 0.04§	7.4 ± 0.04†	7.38 ± 0.04‡
ABG levels with NPPV						
Pa_{O_2}	71 ± 15	71 ± 11	75 ± 18	74 ± 15	80 ± 10	76 ± 15
Pa_{CO_2}	50 ± 6	42 ± 7	44 ± 10	41 ± 8	37 ± 6	42 ± 6
pH	7.39 ± 0.04	7.42 ± 0.04	7.45 ± 0.08	7.4 ± 0.03	7.47 ± 0.06	7.41 ± 0.05
Patients with Pa_{CO_2} > 45 mm Hg without NPPV	45 (78)	41 (58)	18 (78)	14 (50)	6 (50)	16 (84)
Patients with Pa_{CO_2} > 45 mm Hg with NPPV	40 (68)	14 (20)	10 (43)	4 (14)	2 (17)	3 (16)

*Values given as mean ± SD or No. (%).
†$p < 0.001$ (paired t test with vs without NPPV).
‡$p < 0.05$ (paired t test with vs without NPPV).
§$p < 0.005$ (paired t test with vs without NPPV).
‖$p < 0.01$ (paired t test with vs without NPPV).

symptoms and pulse oximetry, polygraphy (Autoset; ResMed; North Ryde, Australia), or polysomnography.

The post-tuberculosis (TB) group (called the *TB group*) included 23 subjects who had all experienced parenchymal and/or chest wall sequelae of TB with or without sequelae of collapsetherapy or thoracoplasty.

The NM diseases group (called the *NM group*) included 28 subjects who had a heterogeneous group of neurologic disorders (Table 3).

The POLIO group included 12 patients who had experienced POLIO.

The kyphoscoliosis (KYPH) group included 19 patients who had experienced either major chest wall deformity with KYPH or rare disorders, such as amelia and agenesis of the homolateral hemithorax (one patient) or severe post-traumatic chest wall mutilation (one patient).

The values reported in Tables 1 and 2 were collected during the patient's first elective evaluation while in a stable clinical condition, a mean duration of 7 ± 4 months after starting NPPV therapy.

Table 3—*Diagnoses of 28 Patients Treated by Noninvasive Ventilation for Neuromuscular Disorders and Chronic Hypoventilation*

Disease	Patients, No.
Amyotrophic lateral sclerosis	6
Duchenne muscular dystrophy	3
Dystrophia myotonica (Steinert muscular dystrophy)	2
Progressive muscular dystrophy	3
Bilateral diaphragmatic paralysis	3
Progressive infantile spinal amyotrophy	2
Other myopathies	6
Syringomyelia	2
Central apnea	1

Pulmonary Function Tests and ABG Levels

The results of pulmonary function tests for each diagnostic category are given in Table 1. ABG levels are shown in Table 2 and in Figure 1. As suggested by the normal pH values, values were obtained during elective medical evaluations, while the patient was in a stable condition. The values for Pa_{O_2} (Table 2) were recorded with usual oxygen flow, when prescribed, with and without ventilator. For all groups, the use of a ventilator significantly decreased Pa_{CO_2} and, albeit for NM subjects, increased Pa_{O_2} (Fig 1, Table 2). The COPD group had the highest values of Pa_{CO_2}. Indeed, all COPD patients had a Pa_{CO_2} ≥ 55 mm Hg when the decision to institute NPPV was made, as emphasized in a 1999 consensus report.[34] Furthermore, the correction of Pa_{CO_2} levels with NPPV, although significant, was not as efficient as in the other diagnostic groups. The correction of Pa_{O_2} level was, however, satisfactory for all patients.

The number of patients with a resting Pa_{CO_2} of > 45 mm Hg, with or without use of a ventilator, is specified in Table 2. Although ventilator adjustments that aimed to obtain the optimal daytime ABG values with NPPV, the correction of hypercapnia was, in some cases, limited by patient tolerance or by leaks either around the interface or through the mouth. Persistent hypercapnia while receiving NPPV therapy occurred only in a minority of patients. However, moderate hypercapnia without NPPV therapy occurred more frequently.

Health Status (Karnofsky Score), Dyspnea, and Scores for Emotional Disturbances

The mean Karnofsky scores were slightly lower for patients with COPD (6 ± 2), TB (6 ± 2), and NM (6 ± 2) than for patients with OHS (7 ± 1), POLIO (7 ± 2), or KYPH (7 ± 1) [*ie*, COPD, TB, and NM

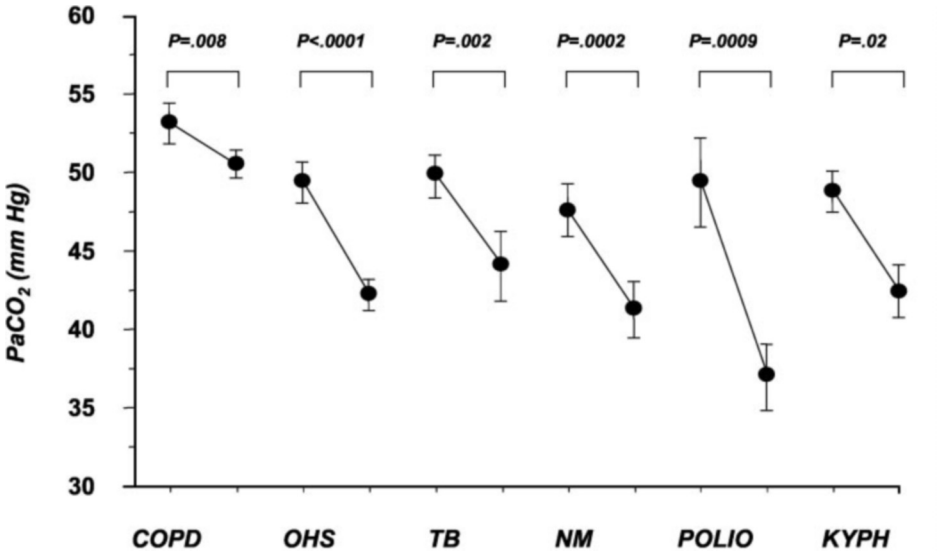

FIGURE 1. Mean $PaCO_2$ values in patients with and without NPPV, per diagnostic group. p Values were determined by paired *t* tests, comparing $PaCO_2$ in patients with and without NPPV.

patients were, on average, more dependent in terms of health status]. Sixteen patients (7.5%) had Karnofsky scores of ≤ 4 (*ie*, they needed assistance equivalent to that dispensed in a hospital). Conversely, 35 patients (17%) had scores of ≥ 8 (*ie*, they were capable of being gainfully employed and of performing normal activities without the need for any special medical care). The mean resting dyspnea scores describe the presence of either very slight or slight resting dyspnea.

Average values for HAD scores (anxiety, 4.7 ± 3.9; depression, 5.6 ± 4) were well within normal limits. Thirteen patients (6%) had scores that were suggestive of anxiety disorders (> 10), and 18 patients (8.5%) had scores that were suggestive of depression (> 10). These results are similar to previously published data in patients receiving HMV[35] or in the general population.[36]

Compliance With NPPV

Effective daily use of ventilator was available for 178 patients (84.4%). Self-reported daily use was not taken into account (Table 4).

The average daily use of NPPV per diagnostic group is shown in Table 4. Daily use was on average significantly higher in the TB and POLIO groups than in the KYPH, COPD, and OHS groups ($p < 0.05$ [unpaired *t* tests]). The difference was not significant for the NM group. For all patients, the mean daily use of ventilator was 6.9 ± 3.4 h per day over the whole study period.

Interruptions of NPPV Because of Noncompliance

Table 4 reports the number of patients who interrupted NPPV therapy because of noncompliance (14 patients; 6.6%) per diagnostic group.

Noncompliance Defined as Average Daily Ventilator Use < 3.5 h per day

A total of 23 patients (13%) used their ventilator < 3.5 h per day (Table 4). Six of these 23 patients (26%) eventually stopped receiving NPPV therapy completely. When combining the patients who interrupted NPPV for noncompliance and the patients

Table 4—*Average Daily Use of Ventilator (Based on Built-In Ventilator Timers), Interruptions of NPPV, and Noncompliance Rates*

Variables	COPD (n = 58)	OHS (n = 71)	TB (n = 23)	NM (n = 28)	POLIO (n = 12)	KYPH (n = 19)
Patients from whom data was obtained, No. (%)	43 (74)	56 (79)	20 (87)	27 (96)	10 (83)	18 (95)
Ventilator use, h/d						
Mean ± SD	6.6 ± 3.9	6.2 ± 2.5	9.1 ± 4.8	7.2 ± 2.9	8.6 ± 2.8	6.2 ± 3
Median	6.7	6.3	8.4	8.1	8.3	6.9
Maximal	22	12.6	22.4	11.8	12	10.4
Patients using their ventilator < 3.5 h/d, No. (%)	8 (19)	8 (14)	0	3 (11)	1 (10)	3 (17)
Interruptions for noncompliance, No. (%)	4 (7)	7 (10)	0	1 (4)	0	2 (10)

who used their ventilator < 3.5 h per day, 31 patients (14.7%) could be considered to be noncompliant.

Compliant vs Noncompliant Patients

When comparing compliant and noncompliant patients, no significant difference was noted in terms of age ($p = 0.84$ [unpaired *t* test]), BMI ($p = 0.80$), FEV_1 ($p = 0.52$), FVC ($p = 0.42$), FEV_1/FVC ratio ($p = 0.41$), PaO_2 without ventilator use ($p = 0.22$), PaO_2 with ventilator use ($p = 0.32$), $PaCO_2$ without ventilator use ($p = 1.0$), $PaCO_2$ with ventilator use ($p = 1.0$), distance covered during a 6-min walk test ($p = 0.57$), dyspnea ($p = 0.65$), HAD scores (anxiety, $p = 0.55$; depression, $p = 0.09$), or functional status ($p = 0.61$). The only significant differences between groups were higher mean values for PImax and PEmax in the noncompliant group (PImax, $p = 0.03$; PEmax, $p = 0.03$), which was a probable consequence of the higher compliance rates in the TB, POLIO, and NM groups, which had the lowest PImax and PEmax values.

The technical aspects of ventilation are summarized in Table 5. Among patients using bilevel ventilators, NM group patients had lower inspiratory positive airway pressure values (to minimize leaks due to the decreased muscle tone of facial muscles in diseases such as amyotrophic lateral sclerosis) and OHS group patients had higher expiratory positive airway pressure values because of the high number of patients with associated OSAS. Supplemental oxygen was required for 101 patients (48%). Patients were equipped either with standard commercialized nasal silicone interfaces (Silicon Contour and Profile Lite; Respironics; Murrysville, PA; or Mirage and Ultra Mirage; ResMed) or custom-molded masks (Lyon model; SEFAM; Nancy, France). One patient only used a facial mask (Full Face; Respironics) on a long-term basis.

Changes in Indications for NPPV During the Study Period: Figure 2 shows, over the duration of the study period, a marked increase in the proportion of patients with COPD (0 to 25%; $p < 0.001$) and OHS (14 to 39%; $p < 0.001$). During the study period, 29% of patients who started receiving NPPV had OHS, 22% had COPD, 11% had NM diseases, 14% had TB, 8.5% had KYPH, and 7% had POLIO.

Changes in Technical Equipment During the Study Period

Between 1992 and 2000, there was a progressive shift in the choice of ventilators (Fig 3). In 1992, all patients were equipped with volume-cycled ventilators (PLV 100; Lifecare; Lafayette, CO; PV 501; Breas; Mölndal, Sweden; or Drägger EV 800; Carbamed; Lausanne, Switzerland). In 1993, bilevel pressure-cycled ventilators became available and were, as of 1994, the most frequently prescribed home ventilators. Over the whole study period, 62% of patients studied were treated with bilevel pressure-cycled ventilators (BiPAP S or ST; Respironics; VPAP II and II/ST; ResMed; PV101 or 102; Breas; or Moritz; MAP; Martinsreid, Germany). The type of ventilator used in each diagnostic category is detailed in Table 5. In 1998, a high-performance pressure-cycled ventilator (PV401; Breas) was commercialized and was used mainly to improve the correction of hypercapnia in patients who had achieved unsatisfactory results using conventional bilevel pressure-cycled ventilators (Table 5).

Table 5—*Type of Ventilator Used by Diagnostic Category and Ventilator Settings

Variables	COPD (n = 58)	OHS (n = 71)	TB (n = 23)	NM (n = 28)	POLIO (n = 12)	KYPH (n = 19)	Total (n = 211)
Volume-cycled ventilators							
Patients	10 (17)	7 (10)	18 (78)	12 (43)	9 (75)	10 (53)	66 (31)
VT/kg, mL	13 ± 4	7 ± 1	12 ± 4	11 ± 4	13 ± 3	12 ± 3	
Total $\dot{V}E$, L	15 ± 4	18 ± 5	16 ± 4	12 ± 3	14 ± 4	12 ± 2	
Respiratory frequency	22 ± 2	21 ± 4	22 ± 5	18 ± 2	18 ± 4	21 ± 5	
Pressure-cycled ventilators							
Number of patients	44 (76)	58 (82)	3 (13)	15 (54)	2 (17)	9 (47)	131 (62)
S mode/ST mode ratio, % of total	69/31	62/38	0/100	53/47	0/100	55/45	
IPAP (cm H_2O)	17 ± 3	18 ± 3	17 ± 2	13 ± 3	14 ± 3	17 ± 4	
EPAP (cm H_2O)	4 ± 2	7 ± 3	3 ± 1	3 ± 1	3 ± 1	3 ± 1	
Respiratory frequency (ST mode)	14 ± 2	14 ± 2	14 ± 2	14 ± 3	13 ± 4	13 ± 2	
Pressure support (Breas PV 401)							
Number of patients	4 (7)	6 (8)	2 (8)	1 (3)	1 (8)	0	14 (7)
IPAP	28 ± 9	24 ± 7	17 ± 2	22	17		
Respiratory frequency	14 ± 1	15 ± 3	15 ± 7	12	12		

*Values given as mean ± SD or No. (%), unless otherwise indicated. VT = tidal volume; $\dot{V}E$ = minute ventilation; IPAP = inspiratory positive airway pressure; EPAP = expiratory positive airway pressure.

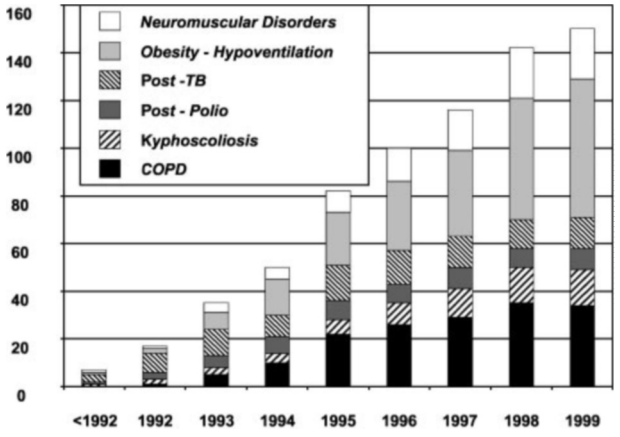

FIGURE 2. Yearly count of the cumulative population of patients treated by NPPV during the study period (1992 to 2000), by diagnostic category.

Pressure-Cycled vs Volume-Cycled Ventilators

Kaplan-Meier curves were computed to compare the probability of pursuing NPPV and survival in patients using pressure-cycled vs volume-cycled home ventilators during the study period (Fig 4). No significant difference was noted between patients using either type of ventilation for the probability of pursuing NPPV ($p = 0.31$ [log rank test]) or survival ($p = 0.71$). Daytime $Paco_2$ levels without ventilator were similar for both groups (volume-cycled ventilators, 50 ± 8 mm Hg; pressure-cycled ventilators, 50 ± 8 mm Hg; $p = 0.44$). $Paco_2$ levels with a ventilator were, however, slightly lower using volume-cycled ventilators (mean $Paco_2$ with ventilator, 42 ± 9 vs 46 ± 8 mm Hg, respectively). Noteworthy is the fact that most COPD patients (those with the highest $Paco_2$ values) were using bilevel pressure-cycled ventilators, thus increasing the mean $Paco_2$ values for patients receiving pressure-cycled ventilation.

Probability of Pursuing NPPV and Survival by Diagnostic Category

Data that are relevant to the use of NPPV and survival per diagnostic group are given in Table 6. The probability of pursuing NPPV was computed after excluding patients who were lost to follow-up (analysis based on 199 patients). For survival analysis, patients interrupting HMV therapy for other reasons than death or patients lost to follow-up were excluded from the analysis (analysis based on 174 subjects) [Table 6, Fig 5].

Days Spent in Hospital for Cardiac and/or Respiratory Illnesses

This analysis was performed on patients from the Geneva area (109 patients), because of the availability of centralized computer records of hospital stays. For the analysis in Table 7, patients were subdivided according to length of follow-up. Table 7 shows a significant decrease in the number of days spent in the hospital per year when comparing the year before NPPV was begun to the years after NPPV was begun (Friedman test or Wilcoxon test).

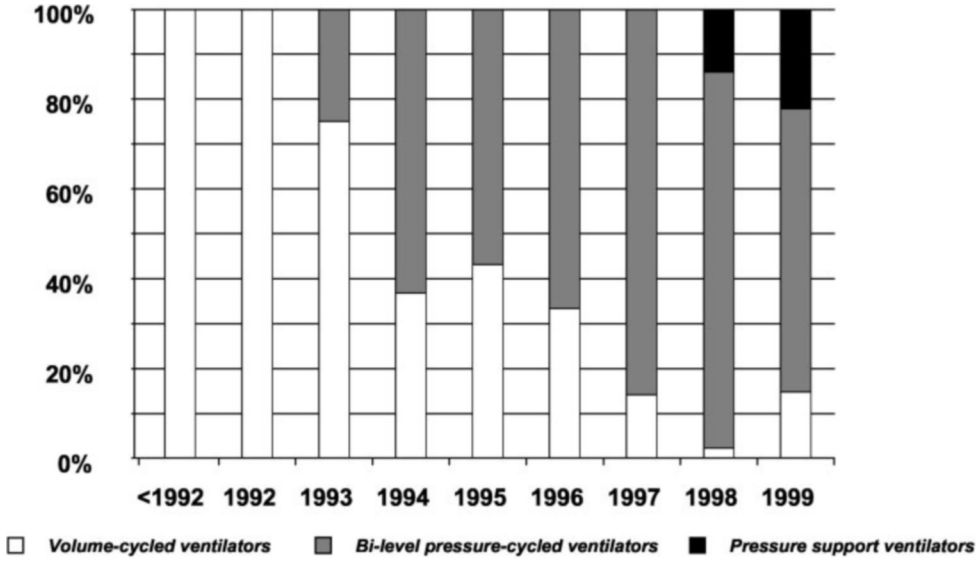

FIGURE 3. Yearly prescription of ventilators during the study period (1992 to 2000). The proportions of volume-cycled ventilators (white bars), bilevel pressure-cycled ventilators (gray bars), and pressure-support ventilators (Breas PV 401; Megamed AG) [black bars] are shown.

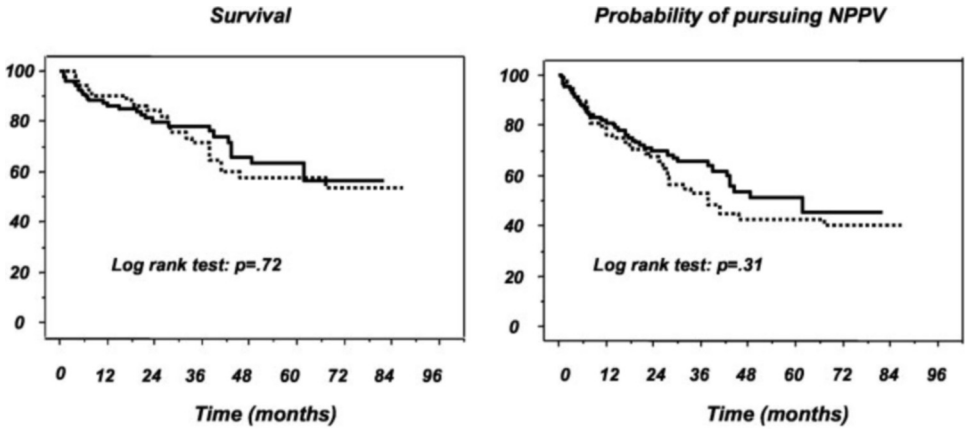

FIGURE 4. Kaplan-Meier curves (with results of log rank test) of survival (*left*; 174 patients) and the probability of pursuing ventilation (*right*; 199 patients) comparing patients using volume-cycled ventilators (continuous line) and those using pressure-cycled ventilators (dotted line).

Three Subgroup Analyses Performed

COPD Patients: After the exclusion of patients who were awaiting transplantation, 24 patients were analyzed. There was a significant reduction in the number of days spent in the hospital for cardiac or respiratory illness when comparing the year before NPPV therapy had begun (mean [± SEM], 42 ± 9 days; 24 patients) with the first year after NPPV therapy had begun (mean [± SEM], 22 ± 5 days; p = 0.02 [Wilcoxon test]; 24 patients) or the second year after NPPV had begun (mean [± SEM], 22 ± 7; p = 0.03; 18 patients). After 3 years, the difference was no longer significant (mean [± SEM], 37 ± 14; p = 0.30; 12 patients).

Patients With Restrictive Disorders (non-COPD): This group included 77 patients. The number of days spent in the hospital decreased significantly between the year before NPPV therapy had begun (mean [± SEM], 22 ± 2 days, median, 17 days; 76 patients) and the 5 subsequent years after NPPV therapy had begun (year 1: mean [± SEM], 17 ± 4 days; median, 6 days; p = 0.009 [vs year before NPPV, Wilcoxon]; 76 patients; year 2: mean [± SEM], 6 ± 3 days; median, 0; p < 0.0001; 57 patients; year 3: mean [± SEM], 6 ± 2 days; median, 0 days; p < 0.0001; 48 patients; year 4: mean [± SEM], 10 ± 4 days; median, 0 days; p = 0.003; 35 patients; and year 5: mean [± SEM], 7 ± 3 days; median, 0 days; p = 0.005; 26 patients).

Patients With OHS: Thirty-two patients were analyzed. The number of days spent in the hospital decreased significantly between the year before NPPV therapy had begun (mean [± SD], 26 ± 4 days; median, 22 days; 32 patients) and the 3 subsequent years (year 1: mean, 17 ± 5 days; median,

Table 6—*Causes of Interruption of NPPV*

Variables	COPD (n = 58)	OHS (n = 71)	TB (n = 23)	NM (n = 28)	POLIO (n = 12)	KYPH (n = 19)
Interruptions of NPPV, No. (% of total)	36 (62)	15 (21)	13 (56)*	8 (29)	6 (50)	6 (31)
Probability of pursuing NPPV,† %						
3-year	49	76	57	78	61	71
5-year	28	72	40	70	40	71
Survival rate,‡ %						
3-year	60	88	63	88	67	79
5-year	35	88	46	79	45	79
Deaths, No. (% of total)	23 (40)	4 (6)	11 (48)	3 (11)	5 (42)	3 (16)
Transplantations, No. (% of total)	6 (10)	0	0	0	0	0
Tracheostomies, No. (% of total)	0	0	1 (4)	0	1 (8)	0
Noncompliance, No. (% of total)	4 (7)	7 (10)	0	1 (4)	0	2 (11)
Lost to follow-up, No. (% of total)	3 (5)	4 (6)	0	4 (14)	0	1 (5)

*One interruption because of ischemic cerebrovascular event.
†Analysis based on 199 patients.
‡Analysis based on 174 subjects.

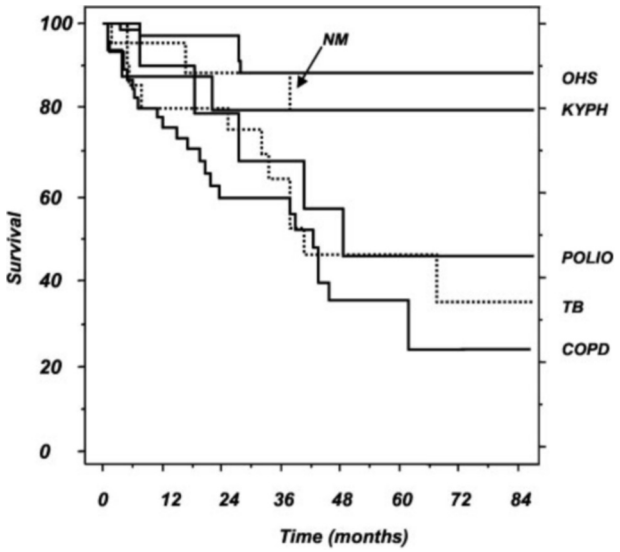

FIGURE 5. Kaplan-Meier curves for survival for patients receiving NPPV therapy by diagnostic category (based on data from 174 subjects, after the exclusion of patients who were lost to follow-up or had interrupted NPPV therapy for reasons other than death). The values for survival after 3 and 5 years per diagnostic group are detailed in Table 6.

9 days; $p = 0.02$; 32 patients; year 2: mean, 3 ± 1 days; median, 0 days; $p < 0.0001$; 25 patients; year 3: mean, 9 ± 4 days; median, 0 days; $p = 0.001$; 22 days), then increased slightly (year 4: mean, 15 ± 9 days; median, 0 days; $p = 0.15$; 14 days).

DISCUSSION

The present study illustrates the changes that have occurred in home NPPV in the Geneva Lake area since the publication of the studies by Leger et al[20] and Simonds and Elliott.[19] Bilevel pressure-cycled ventilation has become the default mode of ventilation in most indications (Fig 3), with results similar to volume-cycled ventilation in terms of the correction of daytime hypercapnia, survival, probability of pursuing NPPV (Fig 4), and a major reduction in cost (prices of volume-cycled ventilators used in study, $11,400 to $13,850; pressure-cycled ventilators, $3,070 to $1,1870 [in US dollars]). Furthermore, the two major indications for NPPV therapy have gradually become COPD and OHS, whereas the number of patients treated for restrictive parenchymal or chest wall diseases, or NM diseases either has remained stable or has showed only a modest increase (Fig 2). Home NPPV therapy was associated with a significant reduction in hospitalizations in all groups studied, although this was limited to the first 2 years of treatment in COPD patients. Compliance with treatment was satisfactory (underusers or interruption of therapy for noncompliance, 15%). Scores for emotional disorders and dyspnea suggested that home NPPV therapy is associated with an acceptable health-related quality of life (QOL), with low dyspnea scores and a prevalence of anxiety or depressive disorders similar to that of the general population.[36]

Pressure-Cycled or Volume-Cycled Ventilators for HMV?

Few studies comparing volume-cycled with pressure-cycled ventilators in patients with chronic respiratory failure have been published to date. Two short-term studies found a similar correction of ABG levels[37] and a similar impact on sleep architecture with both types of ventilators.[38] More recently, Schönhofer et al[13] compared volume-cycled NPPV with pressure-cycled bilevel pressure ventilation (BiPAP; Respironics) [1 month each] in patients with chronic respiratory failure. Of the 30 patients included, 20 (67%) had either equal improvement using both ventilators or managed successfully only with bilevel pressure ventilation. Ten patients (33%

Table 7—*Days Spent in Hospital Per Year for Cardiac and/or Respiratory Illness Before and After Initiation of NPPV**

Patients, No.	1 Year Before NPPV	After NPPV							p Value†
		1 Year	2 Years	3 Years	4 Years	5 Years	6 Years	7 Years	
76	20	8‡	0§						< 0.0001
60	19	6§	0§	0§					< 0.0001
44	17	5§	0§	0§	0§				< 0.0001
31	14	4‡	0§	0§	0§	0§			< 0.0001
21	14	6	0§	0§	0§	0§	0		< 0.0001
9	14	3	0‡	0‡	0	0	0	0	0.026

*Data are presented as median values as the function of length of follow-up.

†Friedman test.

‡$p < 0.05$ vs year before NPPV (Wilcoxon test).

§$p < 0.01$ vs year before NPPV (Wilcoxon test).

[*ie*, nonresponders]) had worsening ABG levels with bilevel pressure ventilation. The likelihood of being a nonresponder was not related to the underlying diagnosis.[13]

Data from the present study comparing patients who used volume-cycled vs those who used pressure-cycled ventilators show no differences in survival or in the probability of pursuing NPPV, suggesting a similar efficacy and acceptance by patients (Fig 4). Daytime $Paco_2$ levels without a ventilator were similar in patients using either mode of ventilation, suggesting a similar impact on the correction of ABG levels.

Pressure-cycled ventilators offer several potential advantages. Flow-triggering systems, which are found in most pressure-cycled ventilators, are more sensitive than the pressure-triggering systems incorporated into volume-cycled ventilators. This can decrease inspiratory muscle oxygen consumption by as much as 15 to 20%[39] and can improve synchronization between patient demand and the ventilator. Expiratory positive airway pressure can improve gas exchange in patients with restrictive disorders such as OHS by increasing functional residual capacity, improves ventilation in patients with associated OSAS, and decreases the work of breathing in patients with severe COPD with intrinsic positive end-expiratory pressure.[40] Furthermore, several ventilators offer the possibility of adjusting the time to peak inspiratory positive airway pressure. This has been shown to decrease the work of breathing in patients with restrictive disorders[41,42] and is an important factor for patient comfort.

Interestingly, there are no specific recommendations as to the choice of volume-cycled vs pressure-cycled ventilators in some guidelines for NPPV use in patients with chronic respiratory failure.[24,34] Severely ventilator-dependent patients benefit from the greater alarm capabilities of volume-cycled ventilators.[43] For most patients, however, the choice of the ventilation mode (*ie*, pressure-cycled vs volume-cycled) is made according to the patient's comfort during ventilation and the ability to correct nocturnal and diurnal hypoventilation.[40] The increase in the use of pressure-cycled ventilators appears thus to be a consequence of a similar efficacy in the correction of ABG levels, with frequently improved patient comfort, at a lower cost than volume-cycled ventilators.

Patients With OHS: A Rising Indication for NPPV?

OHS is defined by the presence of extreme obesity and alveolar hypoventilation during wakefulness.[44] OSAS is often but not always associated with OHS.[45] Without adequate treatment, patients with OHS develop cor pulmonale and recurrent episodes of hypercapnic respiratory failure.

Short-term studies have shown that, among obese patients with OSAS and hypercapnic respiratory failure, there is a subgroup of patients who require NPPV (as opposed to continuous positive airway pressure [CPAP]) to correct their ABG levels and to treat symptoms of hypercapnic respiratory failure. These patients have a higher BMI (mean, > 40 kg/m^2), a higher daytime $Paco_2$, and lower daytime Pao_2 or nocturnal Sao_2 than those who can be managed with CPAP alone.[14,15,46,47] Long-term NPPV therapy also was shown to be effective in improving ABG levels and in treating symptoms of hypercapnic respiratory failure in patients with OHS but without severe OSAS (apnea-hypopnea index, < 20).[48]

The finding of a very large group of patients who had OHS and had been treated with NPPV (29% of all patients included in this study) differs from those of most earlier reports. Changes in the prevalence of morbid obesity in Switzerland cannot explain such an increase in patients with OHS. Even though $\cong$ 10% of the adult population has grade II obesity (*ie*, BMI, > 30 kg/m^2), < 0.5% of the population has a BMI of > 40 kg/m^2.[49] Therefore, the increase in the number of OHS patients is probably related to several of the following factors: a greater experience with NPPV acquired over the past 10 years among chest physicians and specialists in intensive care; the demonstration that NPPV is effective in relieving the strain on respiratory muscles in obese patients[50]; a better knowledge of the consequences of morbid obesity on respiratory function and nocturnal breathing by primary care physicians through the wide use of CPAP for patients with OSAS; and therefore a better and earlier identification of patients who may benefit from NPPV therapy. The use of pressure-cycled ventilators in the great majority of patients (90%) and the very significant decrease in the number of hospital stays for cardiac and/or respiratory illness for the 3 years after the use of NPPV therapy had begun, compared to the year before NPPV therapy had begun, suggest that this treatment is cost-effective.

Home NPPV in COPD Patients

Between 1992 and 2000, COPD patients became the second largest group of patients treated by NPPV in our area (Fig 2). This trend is similar to that reported by ANTADIR in France[10] (representing approximately 60% of patients being treated at home for chronic respiratory failure in France). Among 2,632 patients who were treated by NPPV in France in 1998, 922 had COPD (*ie*, 35% of all patients receiving NPPV therapy). National Swiss statistics show a similar trend, although to a lesser degree.[51]

This remarkable increase has occurred without any demonstrated impact of NPPV therapy on the survival of COPD patients.[52,53] NPPV may, however, have an impact on hospitalizations among COPD patients. In the present study, the time spent in the hospital for cardiac or respiratory illness decreased significantly for 2 years in COPD patients following the initiation of NPPV therapy. Although a study effect is possible, most COPD patients were receiving long-term oxygen therapy (LTOT) before being treated with NPPV. In our area, patient care for patients receiving LTOT (as determined by the frequency of outpatient visits and the number of home visits by nurses) is quite similar to that offered to patients receiving NPPV therapy. Other uncontrolled studies also suggest a temporary (*ie*, up to 2 years) but significant impact of NPPV therapy on the number of hospitalizations[20,54] and general practitioner consultations[54] in patients with hypercapnic COPD. Only two randomized controlled studies[52,53] have investigated the impact of NPPV therapy on hospitalization and exacerbation rates in COPD patients, and they yielded conflicting results. In the European multicentric study by Muir et al,[53] hospitalization rates for acute respiratory failure episodes were significantly reduced in the NPPV group. However, in the study by Casanova et al,[52] NPPV had no effect on the rates of exacerbations, hospital admissions, or intubations after 12 months.

Putative explanations for the increase in the use of long-term NPPV therapy in hypercapnic COPD patients are as follows: the possible impact of NPPV on the use of health resources and health-related QOL[55]; the high prevalence of COPD; the increasing availability of NPPV therapy in emergency departments, ICUs, or general medical wards, thus decreasing mortality during acute exacerbations; and the raising of the issue of how to stabilize patients with severe COPD who have recurrent episodes of hypercapnic respiratory failure on a long-term basis.

Consensus statements[16,34] have suggested restricting NPPV therapy to severely hypercapnic patients (*ie*, $Paco_2$, $\geq$ 55 mm Hg) or to unstable patients with $Paco_2$ values between 50 and 54 mm Hg who have experienced recurrent hospitalizations related to hypercapnic respiratory failure.

Conclusion

Noninvasive ventilation has emerged over the past 15 years as a valuable therapeutic option for the long-term treatment of chronic alveolar hypoventilation in patients with restrictive pulmonary disorders and, to a lesser degree in COPD patients, with an acceptable QOL.[35,55,56] Compliance with NPPV therapy in these patients is remarkably high when compared to that with other modes of respiratory assistance such as LTOT or nasal CPAP.[57–60] Tolerance to treatment is also quite good.[61] The available data suggest that NPPV is cost-effective, mainly through a significant reduction in the number of hospitalizations for cardiac or respiratory illness. Cost-effectiveness has improved over the past 10 years through the much wider use of pressure-cycled ventilators, which appear to be in most cases as effective as volume-cycled ventilators for home care and are less expensive.

In Switzerland today, COPD and OHS are the most frequent indications for the use of NPPV therapy. Although there is to date no evidence that NPPV increases survival in COPD patients, it may decrease the number of hospitalizations for cardiac or respiratory failure in patients with hypercapnic COPD for up to 2 years and thus may improve QOL. In very obese subjects with OHS (BMI, $> 35\ kg/m^2$), with or without OSAS, NPPV therapy also has a positive impact on symptoms of respiratory failure, ABG levels, and the number of hospitalizations. The question that remains unsettled is whether NPPV is necessary on a long-term basis for patients with OHS, or whether those patients should be treated either intermittently or for a limited time span.

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