Long-Term Mechanical Ventilation: Recommendations of the Swiss Society of Pulmonology

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Keywords

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Abstract

Long-term mechanical ventilation is a well-established treatment for chronic hypercapnic respiratory failure (CHRF). It is aimed at improving CHRF-related symptoms, health-related quality of life, survival, and decreasing hospital admissions. In Switzerland, long-term mechanical ventilation has been increasingly used since the 1980s in hospital and home care

settings. Over the years, its application has considerably expanded with accumulating evidence of beneficial effects in a broad range of conditions associated with CHRF. Most frequent indications for long-term mechanical ventilation are chronic obstructive pulmonary disease, obesity hypoventilation syndrome, neuromuscular and chest wall diseases. In the current consensus document, the Special Interest Group of the Swiss Society of Pulmonology reviews the most recent scientific literature on long-term mechanical ventilation and provides recommendations adapted to the particular setting of the Swiss healthcare system with a focus on the practice of non-invasive and invasive home ventilation in adults.

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Abbreviation used in this paper

ABG	Arterial blood gases	LVEF	Left ventricular ejection fraction
aPCV	Assisted pressure control ventilation	MIE	Mechanical insufflation/exsufflation device
AEHRF	Acute episode of hypercapnic respiratory failure	MIP	Mouth maximal inspiratory pressure
AHI	Apnea-hypopnea index	mm Hg	Millimeters of mercury
ALS	Amyotrophic lateral sclerosis	MPV	Mouthpiece ventilation
ASV	Adaptive servo ventilation	NIV	Non-invasive ventilation
AVAPS	Average volume-assured pressure support	NMD	Neuromuscular diseases
BMI	Body mass index	ODI	Oxygen desaturation index
BURR	Back-up respiratory rate	OHS	Obesity hypoventilation syndrome
CHRF	Chronic hypercapnic respiratory failure	OLD	Obstructive lung diseases
COPD	Chronic obstructive pulmonary disease	OSA	Obstructive sleep apnea
CPAP	Continuous positive airway pressure	PCV	Pressure controlled ventilation
CSA	Central sleep apnea	PEEP	Positive end-expiratory pressure
CSB	Cheyne Stokes breathing	PEEPi	Intrinsic positive end-expiratory pressure
DMD	Duchenne's muscular dystrophy	PIF	Peak inspiratory flow
EPAP	Expiratory positive airway pressure	PS	Pressure support (=IPAP-EPAP)
ETCO ₂	End-tidal partial pressure of CO ₂	PSG	Polysomnography
FiO ₂	Inspired fraction of oxygen	PSV	Pressure support ventilation
GLS	Geneva Lake Study	PtcCO ₂	Transcutaneous estimation of PaCO ₂
HCW	Health care worker	QoL	Quality of life
HMV	Home mechanical ventilation	RCT	Randomized controlled trial
HOT	Home oxygen therapy	RLD	Restrictive lung diseases
HRQL	Health related quality of life	SNIP	Sniff nasal inspiratory pressure
ICU	Intensive care unit	SRBD	Sleep-related breathing disorders
ILD	Interstitial lung disorders	TPPV	Positive pressure ventilation via tracheostomy
IPAP	Inspiratory positive airway pressure	VC	Vital capacity
IVAPS	Intelligent volume-assured pressure support	VAC	Volume assisted ventilation
kPa	Kilopascal	VCV	Volume controlled ventilation
LTOT	Long-term oxygen therapy	VT	Tidal volume

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Acknowledgments

1. Introduction

Home non-invasive positive pressure ventilation (NIV) appeared in Switzerland in the mid-80s, as in most neighboring countries, shortly after the publication by Sullivan et al. [1] of the successful treatment of obstructive sleep apnea (OSA) by continuous positive airway pressure via a nasal mask (CPAP). In 1990, 24 patients were ventilated non-invasively in Switzerland [2]. Although there are no official national statistics, a reasonable estimation of the trend in prevalence of home NIV can be derived from 2 surveys performed in the Cantons of Geneva and Vaud (Geneva Lake Study; GLS) [3, 4]. Between 2000 and 2018, NIV users increased from 15/10⁵ to 38/10⁵ inhabitants. To put these figures in perspective, use of CPAP in the same area ($\approx$ 20,000 patients treated) is presently 40 times higher (1,552/10⁵ inhabitants) [5]. Conversely, the number of patients on invasive ventilation via tracheostomy remains marginal. These figures are close to those reported by European countries with a national registry: 47/10⁵ inhabitants in Norway (September 2019, Norwegian National registry for long-term ventilation), 33/10⁵ inhabitants in Sweden (2018, Swedevox), and 39.5/10⁵ inhabitants in Finland [6].

1.1. Methodology

The Swiss Society of Pulmonology (SSP) and the Swiss Society of Pediatric Pulmonology have previously published recommendations on home mechanical ventilation (HMV; 1996, 2006, 2010) [7–9]. This narrative review includes the most recent recommendations of our group based on an extensive review of the medical literature through PubMed over the past 10 years, of other national guidelines [10–15], and of the specifics of care for long-term HMV in Switzerland. The final text was discussed thoroughly among the members of the Special Interest Group on HMV (SIG) to reach a consensus.

This text focuses on HMV provided at home or in long-term care institutions and will cover indications, modalities and follow-up of patients on HMV. We will also comment on the use of mechanical insufflation/exsufflation (MIE) devices, and their indication. This document does not cover NIV in the acute care setting (emergency ward, ICU, acute-care hospital wards) or the pediatric population.

1.2. Indications for Long-Term Non-Invasive Ventilation

Indications for long-term NIV, which have evolved over the past 30 years, are summarized in Figure 1 and

Table 1 [16]. The obesity-hypoventilation syndrome (OHS), chronic obstructive pulmonary diseases (COPD; including overlap syndrome), and neuromuscular and chest wall diseases (CWD) are presently the most frequent indications for HMV. Although practices may vary from one Canton (region) or University Hospital to another, trends follow the practices of other European countries.

1.3. General Comments and Caveats

Although patients on long-term home NIV are a very heterogeneous population, they share a certain number of characteristics:

- They often have several comorbidities (most often cardiovascular, cerebro-vascular or neurological disorders) [4].
- They are increasingly overweight or obese [4, 17].
- Mean age of this population is increasing [4, 17].
- Mild or moderate cognitive impairment may coexist with the underlying pathology (i.e., severe COPD [18, 19], advanced amyotrophic lateral sclerosis (ALS) [20–22], some chronic neuromuscular diseases (NMD), very old subjects, sequelae of acute or chronic cerebral traumatic or non-traumatic lesions...).
- They may represent a considerable burden for care providers.

The follow-up of patients on NIV must therefore deal with all these aspects, in close collaboration with primary care physicians and the local healthcare network. Because many of the disorders leading to chronic hypercapnic respiratory failure (CHRF) are rare, the pulmonologist is often referred to as an expert and healthcare coordinator.

1.4. Choice of Ventilators and Ventilator Modes

Table 2 summarizes the ventilator modes most commonly used for long-term NIV [23]. In long-term NIV, bi-level positive pressure support ventilation in spontaneous/timed mode (PSV-ST; Table 2) is presently the most commonly used mode in clinical practice. These recommendations will therefore focus on this mode and will comment on the specifics of other ventilator settings in certain indications. A reminder of the basic settings for PSV-ST is provided in Figures 2 and 3. The reader is also provided with ventilator settings used in Swiss publications as an indication of possible settings (online supplement; see www.karger.com/doi/10.1159/000510086 for all online suppl. material) [4, 24]. Volumetric ventilation is mainly considered in case of failure of PSV or pressure-controlled ventilation (PCV), in some NMD, in very severe OHS, and in difficult cases of patient ventilator

Fig. 1. Mechanisms implicated in chronic hypercapnic respiratory failure.

asynchrony (e.g., paradoxical adduction of vocal cords in ALS) [25]. Volumetric ventilators have been considered historically as “default devices” in invasive ventilation (i.e., ventilation by tracheostomy), although invasive ventilation with PSV and appropriate humidification is clearly feasible if appropriate humidification is ensured [26].

A distinction between ventilators for home care must be made between “Life-support devices” (with EU certification, compatibility with simple or double respiratory circuit and non-rebreathing expiratory valve, built-in battery of >8 h of autonomy and “full range” of alarms including: electrical failure, patient disconnection, high non-intentional leaks, changes in minute ventilation), “Life-sustaining devices” (built-in battery not fulfilling life support criteria, basic range of alarms) and other home care devices (no built-in battery, minimal or no alarms) [27]. Ventilators with a built-in battery are the recommended devices for patients requiring more than 16 h/day of ventilatory support. For these patients (see section 7.1. on dependent patients), prescription of a second ventilator is recommended.

These recommendations will not address the issue of *automated modes* (Table 2). Over the past 15 years, a multitude of automated ventilator modes have been proposed by the industry. This trend started with volume-targeted devices (AVAPS, IVAPS), and complexity increased with the addition of auto-titrating expiratory positive airway pressure (EPAP), pressure support, and backup respiratory rate (BURR) [28–33]. Some devices also provide preset modes for obstructive or restrictive disorders. These modes are the result of a very sophisticated engineering and technical research. They are not however “fail-safe.”

Table 1. Most frequent indications for long-term ventilation

1. Obstructive lung disorders
a. Chronic obstructive pulmonary disease (COPD)
b. Overlap syndrome
c. Diffuse bronchiectasis
d. Bronchiolitis obliterans
e. Cystic fibrosis
2. Obesity-hypoventilation syndrome
3. Restrictive chest wall and parenchymal disorders other than obesity-hypoventilation
a. Kyphoscoliosis and other chest wall deformities
b. Ankylosing spondylitis
c. Chest trauma
d. Sequelae of tuberculosis and/or thoracoplasty and/or thoracic surgery for cancer
e. Restrictive pleural diseases
4. Neuromuscular disorders (see Table 4)
5. Sleep-related breathing disorders
a. Obstructive sleep apnea
b. Central sleep apnea

This table does not provide all indications for NIV: it lists the most frequent and common indications within the diagnostic categories provided.

None of these options has, to date, been proven superior to conventional titration of bi-level PPV [28, 32, 34–40]. They are at best “non-inferior” to individually titrated settings. They may have a favorable impact on time needed to reach satisfactory ventilator parameters in some clinical settings.

Table 2. Ventilator modes available on most devices used for home noninvasive ventilation (adapted from Schwarz and Bloch [23])

Abbreviation	Mode	Settings*
CPAP	Continuous positive airway pressure	CPAP pressure with additional options according to manufacturer
PSV-S	Pressure support ventilation, spontaneous mode	IPAP, EPAP, TI_{MIN} , TI_{MAX} , sensitivity of inspiratory and expiratory (cycling) triggers, inspiratory rise time, fall time
PSV-ST	Pressure support ventilation, spontaneous/timed mode	IPAP, EPAP, respiratory back-up rate, TI_{MIN} , TI_{MAX} , or fixed TI^{**} ; sensitivity of inspiratory and expiratory (cycling) triggers, inspiratory rise time, fall time
PSV-T	Pressure support ventilation, timed mode	IPAP, EPAP, respiratory frequency, TI_{MIN} , TI_{MAX} , or fixed TI , sensitivity of expiratory (cycling) trigger, inspiratory rise time, fall time
(a)PCV	(Assisted) pressure control ventilation	IPAP, EPAP, respiratory frequency or respiratory back-up rate (in assisted mode), TI ($TI:TE$), sensitivity of inspiratory trigger (in assisted mode), inspiratory rise time, fall time
<i>Automated modes</i>		
iVAPS, AVAPS	Volume-assured pressure support ventilation	Targeted V_T or VA ; minimal and maximal pressure support, EPAP, and respiratory back-up rate

IPAP, inspiratory positive airway pressure; EPAP, expiratory positive airway pressure; TI , inspiratory time; TI_{MIN} , minimal inspiratory time; TI_{MAX} , maximal inspiratory time; TI , fixed inspiratory time; V_T , tidal volume; VA , alveolar ventilation. Fall time refers to time set for passage from inspiratory to expiratory airway pressure (see Fig. 2, top).

* Specific settings for modes described may not be available in all ventilators, depending on manufacturer and device. ** Options for inspiratory time (TI) settings depend on device and mode. Settings for TI may apply to patient-triggered cycles and/or controlled cycles. See text section 1.5.

The SIG group recommends that the use of automated modes is left to the discretion of the clinician, with the following important caveats:

- Automated modes are not presently recommended as a default option.
- Because most of these modes have not been independently validated or proven to be superior to manual titration, the authors recommend having a low threshold for checking the adequacy of NIV by nocturnal polygraphy/polysomnography when using automated modes.

The authors also recommend using modes and devices with which one is familiar, since performance of NIV devices is heterogeneous and devices have their specific algorithms.

1.5. Comments on Specific Ventilator Settings (Table 2)

Ramp or SoftStart options. Several devices for home NIV provide an option allowing a progressive increase in expiratory pressure values and, in some cases, of pressure support ($PS = IPAP - EPAP$). This “comfort option,” derived from the ramp option commonly used for patients treated by CPAP for OSA, can be problematic in patients

under NIV, and even a source of discomfort. If used repeatedly, it can also compromise the efficacy of ventilation. In a recent case series highlighting the drawbacks of this option, the authors discourage the use of this option [41]. If used, initial pressure support should be at least 5–6 cm H_2O , time to attain set pressure should be as short as possible and relevance of this option should be regularly reevaluated [41].

Pre-set decline of pressure support (Soft Stop, Ramp down). This option has been devised for patients with “de-ventilation dyspnea” (i.e., severe transient dyspnea after interruption of ventilation) although it has not been validated in independent clinical studies [42]. The ramp is triggered by the patient prior to his/her interruption of NIV: when activated, pressure support will decline progressively from its preset value to 0, over a predefined time (usually 10–20 min). The ventilator then remains in a CPAP mode at EPAP value until it is stopped by the patient.

Rise time. Figure 2 (top) shows how rise time impacts on pressurization. Short values decrease work of breathing [43] but may be perceived as uncomfortable or cause leaks. In obstructive lung diseases, short rise times (≤ 150 ms) favor a shorter inspiratory time (TI) and a favorable

Fig. 2. Settings for bi-level positive pressure ventilation. PS, pressure support (Δ [IPAP-EPAP]); IPAP, inspiratory positive airway pressure; EPAP, expiratory positive airway pressure; $T_{i_{min}}$, minimal inspiratory time; $T_{i_{max}}$, maximal inspiratory time. Top: impact of changes in rise time and fall time on pressurization. Bottom: Cycling window. Cycling occurs between $T_{i_{min}}$ and $T_{i_{max}}$. Settings subject to variations according to device.

Fig. 3. Cycling settings. PS: pressure support (Δ [IPAP-EPAP]). IPAP: inspiratory positive airway pressure; EPAP, expiratory positive airway pressure; PIF, peak inspiratory flow; P_{AW} , airway pressure. Impact of cycling criterion on pressurization and I:E ratio. A cycling criterion at a high percentage of PIF (top) favors a low I:E ratio, a longer expiration, and is appropriate in obstructive lung disorders. Conversely (bottom), a cycling criterion at a low percentage of PIF favors a higher I:E ratio, prolongs insufflation, and is recommended in restrictive lung disorders such as OHS.

I:E ratio (e.g., $\approx 1:3$). Conversely, rise times of 150–250 ms are commonly used in restrictive lung diseases [4, 14, 24]. Longer rise times may impinge on pressurization time and affect efficacy of ventilation. Values above 300 ms are not recommended albeit for comfort reasons in a newly electively ventilated patient: this value should then progressively be decreased over time.

Inspiratory trigger. In most devices used for long-term ventilation, inspiratory triggers are flow-dependent and very sensitive. Inspiratory trigger sensitivity scales vary according to device and manufacturer: they may be expressed as non-specific descriptors (i.e., high, medium, low), as arbitrary numerical units or as flow (L/min) required to trigger pressurization. Some devices provide algorithms with automated settings (e.g., Autotrak®). Inspiratory trigger sensitivity seldom requires adjusting and can be set by default at mid-range values. Increasing inspiratory trigger sensitivity may be an option in advanced NMD when inspiratory muscles are severely weakened (e.g., advanced ALS or Duchenne muscular dystrophy). In this situation, polygraphic tracings or detailed analysis of ventilator curves may show patient-ventilator asynchrony (e.g., unrewarded inspiratory efforts) [44]. The risk associated with increasing sensitivity is the occurrence of auto-triggering which may be a source of discomfort and affect ventilator efficacy. *In case of unrewarded inspiratory efforts, control of leaks and management of intrinsic positive end-expiratory pressure (PEEPi) should be optimized before adjusting inspiratory trigger* [44, 45]. PEEPi can be compensated by increasing EPAP values, and by optimizing the I:E ratio (decreasing TI and respiratory rate) and cycling criteria.

Expiratory trigger (cycling). Expiratory trigger (or cycling) setting is important for patient comfort, and prevention of patient-ventilator asynchrony and dynamic hyperinflation in COPD [46]. It also contributes to improve V/Q matching in severe restrictive disorders (e.g., obesity-hypoventilation). Bench tests have shown that home ventilators tend to cycle prematurely when submitted to restrictive mechanics conditions, while delayed cycling occurs with default settings in obstructive lung conditions [47]. Cycling should be set at a high percentage of peak inspiratory flow (PIF) in obstructive lung diseases and at a low percentage of PIF in restrictive disorders such as obesity-hypoventilation (Fig. 3). The impact of cycling on the I:E ratio is illustrated in Figure 3.

Inspiratory time. As mentioned in Table 2, options for TI settings vary considerably from one device to another and according to mode. TI may be either allowed to vary in a cycling window between a minimal (TI_{MIN}) and max-

imal value (TI_{MAX}) or set at a fixed value (Fig. 2, bottom). It may also be determined automatically by an algorithm. Some devices distinguish between controlled and triggered cycles and apply TI settings only to one or the other. Clinicians must explore the specific options available on the device they are using. In all cases, TI must be above rise time [48]. A minimal value of 0.5 s is recommended.

Fall time (Fig. 2, top). A few ventilators allow to set the time required for pressure to drop from inspiratory to expiratory set values (i.e., cycling). Manufacturers suggest that this may be used to prevent dynamic hyperinflation and to avoid premature expiratory closing of peripheral airways. This interesting option requires further clinical validation.

1.6. Humidifiers

Roughly 70% of patients on home NIV use heated humidifiers (built-in or add-on) [4]. Humidification decreases dehydration of mucosal membranes, decreases upper airway resistance, and improves airway mucociliary clearance [49, 50]. Although it does add some complexity to the treatment, it is recommended to add active humidification with a low threshold. Use of distilled or demineralized water is recommended, with daily changing, and rinsing/washing of container.

1.7. Tubings, Circuits and Filters

Respiratory circuits (i.e., the tubing between the ventilator and the interface or tracheal canula) are either single- or double-limb (Fig. 4).

Double-limb circuits are mostly used in acute care settings (ICU) [23, 51]. One tube is for inspiration, the other for expiration. Active unidirectional valves redirect exhaled air through the expiratory circuit towards the respirator thus avoiding any risk of rebreathing. These circuits (and associated interfaces) are non-vented (i.e., without exhalation port). A minimal expiratory flow (PEEP or EPAP) is not required to prevent CO₂ rebreathing, and thus PEEP can be set at 0. Double-limb circuits allow direct measurement of expired volume (VE). Inspiratory and expiratory tubes may be coaxial: this allows passive heating of the inspired gas by expiratory flow.

For home ventilation, **single-limb circuits** are most commonly used [23, 51]. They are less cumbersome. To prevent CO₂ rebreathing, the circuit must have either an active expiratory valve, placed close to the mask to minimize dead space, or a passive calibrated exhalation port (i.e., a passive leak valve) which can be either integrated in the interface (vented mask) or in the circuit (vented circuit). The active valve opens only during expiration.

Fig. 4. Tubings. **a** Double-limb circuit with unidirectional valve to avoid rebreathing, non-vented mask, and expiratory valve built in the ventilator. **b** Single-limb circuit with active expiratory valve and non-vented mask. **c** Single-limb circuit with passive exhalation port (on tubing, close to non-vented mask). **d** Single-limb circuit with passive exhalation port incorporated into vented mask. **e** Coaxial tubing, unvented mask, and expiratory valve built in the ventilator.

The passive port creates an intentional continuous air leakage and requires a minimal expiratory pressure (usually 3–4 cm H₂O) to prevent rebreathing and flush the CO₂ from the circuit. Because of their ease of use, vented masks are most often used for home NIV. One disadvantage of using a single-limb circuit is that unintentional leaks and tidal volume (VT) provided by ventilator software are estimated and not measured. Bench studies have shown that VT (and therefore VE) is most often underestimated [52–54], with a high variability in bias reported (66–236 mL reported by Contal et al. [53]). In case of unintentional leaks, however, VT may be overestimated. The precision of the estimation of VT is not only influenced by unintentional leaks but also by the breathing pattern and the underlying lung mechanics: in one bench-test study, underestimation was more important in obstructive than in restrictive settings [52]. This may inter-

fere not only with monitoring of VT but also with the performance of ventilators in volume-targeted modes [52].

Mouthpiece ventilation (MPV: most often used for daytime ventilation in neuromuscular disorders) can be provided with a single or a double-limb circuit and various types of mouthpieces [55–57]. Articulated support arms which can be fixed to wheelchairs are commercialized and allow easy positioning of mouthpiece. Recent multimodal ventilators provide either volume-cycled or pressure-cycled dedicated modes for MPV, and do not require exhalation valves.

Heated tubings may improve patient comfort and efficacy of NIV when using a heated humidifier. Although heated and humidified air can improve airway mucociliary clearance, management of secretions, and decrease upper airway resistance [49], condensation may cause pa-

Fig. 5. Interfaces for noninvasive ventilation. **a** Oro-nasal mask. **b, c** Nasal masks. **d** Facial mask. **e** Detail of exhalation valve of mask. **f** Mouthpiece. From Schwarz and Bloch [23].

tient-ventilator asynchrony, and interfere with pressurization [50]. Heated tubings prevent condensation that may occur when using a heated humidifier. A tissue hose around the tubing can also decrease the temperature gradient and prevent condensation in ventilator tubing.

Antibacterial filters are recommended when using the same ventilator for different patients (hospital setting). For home NIV, there is no formal recommendation as to their use. Heat- and moisture-exchanging filters may prevent mucosal dryness when the use of an electrically heated humidifier is not feasible, such as during travel or ambulation.

Supplemental oxygen is provided by an oxygen blender in most hospital (ICU) ventilators. For home NIV, oxygen is added to the breathing circuit when needed. In this setting, effective oxygen delivery and FiO_2 depend not only on oxygen flow but also on intentional and unintentional leaks, site of oxygen administration on ventilator circuit, site of exhalation port, ventilator settings and re-

spiratory drive [58]. There is thus no simple relation between oxygen requirements at rest without NIV and oxygen flow required on the ventilator circuit, and titration of oxygen flow requires monitoring of SpO_2 . When the circuit is vented, the highest oxygen concentration is achieved with oxygen added to the mask: this may be relevant in rare situations of very high FiO_2 requirements [58]. In other cases, the most appropriate site of oxygen adjunction is close to the ventilator, which improves comfort. Certain homecare ventilators have a special oxygen port for connection of the tubing from a low-pressure oxygen source such as an oxygen concentrator. This port closes automatically if the ventilator is turned off thereby preventing the risk of fire hazard by continuous oxygen flow into an inactive ventilator. Oxygen flow must be titrated by pulse oximetry or arterial blood gas analysis.

Aerosols can be delivered during NIV. With a single-limb circuit, vibrating mesh nebulizers are more efficient than jet nebulizers. They must be placed as close as pos-

sible to the mask, between the mask and the exhalation port [59, 60].

1.8. Interfaces

The number of interfaces made available by the industry is constantly increasing, providing more and more options for improving patient comfort. It is important to work with healthcare providers or healthcare workers who are up to date with the most recent interfaces. At present, facial masks are the most widely used in published data concerning long-term NIV [4, 61–63]. However, there is an increasing awareness of the caveats associated with facial masks, that is, an increase in upper airway resistance caused by retro-pulsion of the jaw, which may induce or prevent the correction of upper airway obstruction [25]. Oro-nasal masks (Fig. 5) are being increasingly used, are less cumbersome, and may be an alternative to facial masks either because of pressure sores on the nose or claustrophobia. Although nasal masks may favor mouth leaks during the night, this can be at least partially prevented by the use of chin straps that secure the position of the jaw although they cannot prevent leaks at the lips. Nasal prongs are a useful option for daytime ventilation, for situations requiring low pressure support, although they may tolerate up to 25 cm H₂O of inspiratory pressure. Mouthpiece ventilation is also an excellent option for daytime ventilation in NMD. Custom-made masks are seldom required.

Hygiene of masks is critical, is important for prevention of skin lesions and leaks and requires repeated education for patients and caregivers. All parts of the mask, especially the cushion and the ventilation port (exhalation valve), should be cleaned after each use with lukewarm water and mild soap.

1.9. Where, How and by Whom Should Home NIV Be Implemented and Followed?

In Switzerland, long-term HMV, irrespective of the diagnosis or setting, must be prescribed by a certified pulmonologist who can initiate the treatment and provide appropriate instruction to the patient and caregivers. The indication for HMV is usually reviewed by the medical advisor of the medical insurance.

Data from the GLS provide an indication as to actual practices in Switzerland for home NIV [4], which may evolve.

- Half of all long-term NIV treatments are started electively, and half in an emergency setting.
- Roughly 80% of all patients start their treatment as inpatients (electively or after an acute exacerbation).

- On a long-term basis, in the GLS study, 1/3 of all patients were followed exclusively by a pulmonologist in private practice. Thus 2/3 of long-term NIV patients were followed by a hospital with or without a pulmonologist in private practice.

The role of healthcare providers and pulmonologists in private practice as actors in home NIV is increasing in Switzerland. This practice differs from that of several European countries. In the Netherlands, in Germany, in Denmark, or in Norway for instance, patients on long-term NIV are treated and followed exclusively by expert hospitals.

The SIG suggests the following recommendations:

- *The goal of NIV is to improve symptoms and health-related quality of life, decrease hospital admissions, correct hypoventilation, and optimize SpO₂ to improve survival, prevent cardiovascular complications such as pulmonary hypertension and cor pulmonale. If nocturnal PtcCO₂ and sleep-related breathing disorders (SRBD) are controlled, but SpO₂ remains low, addition of oxygen on the ventilator circuit may be considered.*
- *Elective implementation of NIV may be performed in a hospital, in an outpatient clinic, or at the patient's home by an experienced team (healthcare provider) led by an experienced pulmonologist [64, 65].*
- *Outpatient initiation of NIV is a possible option in stable patients. It can be recommended for example in patients with a prior experience of CPAP, and in elective situations of patients with SRBD, OHS, or NMD, with monitoring of blood pressure and SpO₂ under NIV and follow-up of arterial or transcutaneous CO₂ (PtcCO₂).*
- *Frequency of follow-up evaluations (modalities, timing) depends on the underlying pathology, and is usually performed every 3–12 months. A follow-up evaluation is in most cases recommended at least once a year.*
- *Modalities of follow-up have been reviewed in detail by the SomnoNIV group (see Fig. 6) [66] and include clinical examination, targeted medical history, arterial blood gases (ABG), nocturnal pulse oximetry, downloading and analysis of ventilator software, and, when indicated, more detailed sleep studies or lung function tests.*
- *When available, use of nocturnal transcutaneous CO₂ measurement is recommended, preferably at the patient's home, especially in subjects under oxygen therapy or with persistent diurnal hypercapnia [66–68].*

Fig. 6. Proposed algorithm for monitoring patients under long-term NIV. Adapted from Janssens et al. [66].

1.10. Tools for Measuring ABG

Correction of ABG and more specifically, of diurnal and nocturnal PaCO_2 and respiratory acidosis, is one of the main goals of long-term mechanical ventilation. Measurement of daytime ABG, most often through puncture of the radial artery, is considered as a gold standard procedure. However, it has its drawbacks: it may be painful, awakens the patient if performed at night, and requires expertise. Furthermore, it is only representative of the moment when sampling was performed and does not actually reflect the time course of PaCO_2 during the night [66].

Alternative tools may provide useful information as to ABG while decreasing patient discomfort.

- *Capillary arterialized samples* are usually taken at the earlobe after application of a vasodilating gel. They have been reported as reliable for pH and PaCO_2 , with only small biases and limits of agreement in patients with various pulmonary disorders and in a meta-analysis [69, 70]. Results for PaO_2 are less reliable, with an overall underestimation of arterial PaO_2 by the capillary technique [69, 71]. Capillary samples require fur-

ther validation in a population of subjects with CHRF [72, 73].

- *End-tidal CO_2* : Although routinely used by anesthesiologists during surgical procedures, the reliability of ETCO_2 as a surrogate of ABG is insufficient. ETCO_2 systematically underestimates PaCO_2 . Agreement between PaCO_2 and ETCO_2 values is affected by V/Q mismatch, by physiological dead space, by pulmonary vascular disorders and by ventilatory mode (expiration time) and thus values provided by ETCO_2 are considered unreliable in adult populations [74]. It must be emphasized that a normal ETCO_2 does not exclude hypercapnia, whereas a high ETCO_2 is strongly suggestive of hypercapnia, although it may underestimate its severity [66, 74]. The SIG suggests limiting the use of ETCO_2 to special situations, for example, for children with NMD.
- *Transcutaneous capnography (PtcCO_2)*: PtcCO_2 measurements are presently considered reliable in hemodynamically stable patients and use of PtcCO_2 devices has improved in user-friendliness. Devices are non-

- invasive, and well tolerated at a probe temperature of 42°C for 8–12 h [75]. Recent studies have reviewed the performances of several devices and shown that they have acceptable biases and limits of agreement, when compared to ABG, in patients with CHRF treated by long-term mechanical ventilation [67]. There are however a few limitations that the clinician must bear in mind: (1) there is a lag time between changes in PaCO₂ and PtcCO₂ of a few minutes which makes these devices unreliable for the detection of rapid changes in PaCO₂ such as in OSA [76]; (2) most clinical studies show the occurrence of unpredictable errand values which require experience in tracing analysis and may be misleading [66]; (3) in spite of their apparent ease of use, PtcCO₂ devices require a dedicated team with expertise: the number of unreliable traces increases when recordings are not organized by an experienced team.
- The question of defining what is an acceptable definition of nocturnal hypoventilation has been arbitrarily solved by expert-based suggestions published by the American Association of Sleep Medicine [77]. This subject is however still open to discussion, and minor changes in definitions of hypoventilation can have a substantial impact in clinical practice [78, 79].

1.11. Frequent Side Effects of Mechanical Ventilation and Their Management

On average, NIV is remarkably well tolerated. Adherence to treatment documented in recent Swiss studies, suggests that side effects are rarely important enough to compromise the pursuit of the treatment [4, 24].

A symptom-based pragmatic 11-item questionnaire targeting NIV-related discomfort has been recently made available for clinical practice (S³-NIV questionnaire) [80].

Table 3 lists the most frequent side effects reported on NIV. Appropriate humidification and management of leaks are necessary to correct most causes of discomfort. Repeated education for the patient and caregivers to avoid skin lesions and ensure appropriate positioning of the interface are crucial. Settings must be adjusted to limit leaks and/or prevent abdominal distention and discomfort (i.e., rise time, level of pressure support, cycling criterion...).

A distressing symptom, referred to as “deventilation dyspnea,” is the occurrence of severe dyspnea for minutes to hours after cessation of NIV. This is reported in severe COPD [42] but also in neuromuscular disorders or in obesity-hypoventilation. Specific strategies have been

Table 3. Most frequently reported side effects related to the use of noninvasive ventilation

Patient discomfort resulting from:

- unintentional leaks (around the interface or through the mouth)
- leak-induced xerostomia, xerophthalmia or conjunctival irritation
- pain caused by head gear or mask
- skin lesions, pressure sores and ulcerations
- nasal obstruction, congestion, rhinorrhea, nasal mucosal dryness
- inappropriate alarm settings
- abdominal distention
- perceived patient-ventilator asynchrony (delayed triggering, premature or delayed cycling, autotriggering...)
- disrupted sleep
- claustrophobia or anxiety related to interface

Adapted from Janssens et al. [251].

suggested for COPD: in these patients, deventilation dyspnea may result from progressive dynamic hyperinflation overnight [42]. Mechanisms involved in OHS or neuromuscular disorders are not described. Several home ventilators provide an option of progressive decrease in pressure support before cessation of NIV, triggered by the patient, which warrants further clinical testing.

Side effects related to invasive ventilation are discussed in section 7.4.

2. Obstructive Lung Diseases

2.1. General Comments

Although practices vary widely from one country to another, COPD is either *the* most frequent or among the most frequent indications for long-term NIV in most European countries and represents on average 30% of the long-term NIV population [81, 82]. Acute exacerbation of COPD is the main cause of acute hypercapnic failure requiring ventilatory support in the ICU: 44% of these patients are overweight or obese, and average BMI is 29.8 ± 8.8 kg/m² [83]. In France, data from the multicentric French ANTADIR observatory (www.antadir.org; covering ≈ 7,000 patients under NIV, 2011) document COPD as the second indication for NIV after SRBD. A recent Swiss descriptive study (GLS) showed that, among 489 stable patients on NIV in the cantons of Geneva and Vaud, 190 (39%) had COPD. Median BMI was 28 kg/m² (IQR 21; 33) for COPD patients without OSA (*n* = 135), and 32

Fig. 7. Suggested algorithm for noninvasive ventilation (NIV) in COPD based on references [96, 97, 99].

kg/m² (IQR 28; 40) for those with overlap syndrome ($n = 55$). These data thus show that the *dominant phenotype* among COPD requiring long-term NIV in our area is a population of comorbid frequently overweight or obese patients, with, in one third of cases, associated OSA. This must be kept in mind when analyzing the available evidence regarding long-term use of NIV in COPD.

Short-term studies have shown a benefit of so-called “high intensity NIV” (combining high IPAP values and high BURR) on pulmonary function tests (PFT), 6 min walk tests, ABG, V/Q ratio, and HRQoL when compared to low-intensity NIV [84–86], without any major negative impact on quality of sleep [87]. Noteworthy is the fact that high-pressure NIV may affect cardiac function and must be applied with caution in patients with chronic heart failure, and should thus be initiated under monitoring in a hospital setting [88–90].

After decades of conflicting evidence regarding the long-term benefit and clinical impact of NIV in COPD [91–93], meta-analyses [94, 95], 3 recent randomized-controlled studies [86, 96, 97], and the report of an ERS task force have provided a partial scientific basis for the long-term use of NIV in COPD [98].

In 2014, Struik et al. [94] published a systematic review and meta-analysis, covering data concerning 245 COPD patients from publications compiled up to 2012: *using IPAP levels of at least 18 cm H₂O, using NIV for at least 5*

h per night, and having a baseline PaCO₂ of at least 55 mm Hg (7.3 kPa) were identified as factors predictive of an improvement in ABG [67].

An important Dutch randomized controlled study (RESCUE trial) included COPD patients who remained hypercapnic (PaCO₂ >6 kPa [45 mm Hg]) just after an acute episode of hypercapnic respiratory failure (AEHRF) [97]: 201 COPD patients hospitalized for AEHRF were randomized 48 h after termination of ventilator support to long-term NIV ($n = 101$; PaCO₂: 59.3 ± 9 mm Hg [7.9 ± 1.2 kPa]; FEV₁: $25.6 \pm 7.8\%$ predicted) vs. usual care ($n = 100$; PaCO₂: 57.7 ± 9.7 mm Hg [7.7 ± 1.3 kPa]; FEV₁: $25.7 \pm 8.6\%$ predicted). Average BMI was <25 kg/m² in both groups. One year later, the authors found no significant benefit of NIV on survival, hospital readmissions or HRQL when compared to the control population. Furthermore, PaCO₂ decreased both in the NIV and in the control group. It was concluded that recovering from an AEHRF is not per se a justification for long-term NIV.

A British multicentric RCT (HOT-NIV trial) included 116 COPD patients recovering from an AEHRF with persistent hypercapnia (PaCO₂ >53 mm Hg, 7.1 kPa) 2–4 weeks following an acute hypercapnic exacerbation requiring NIV [99]. Patients with a BMI >35 kg/m², OSA, or other causes of CRF (NMD, CWD) were excluded. Patients were randomized to home oxygen therapy

(HOT) versus HOT and high-intensity NIV. NIV increased the time to hospital readmission by approximately 3 months (4.3 months [IQR 1.3–13.8] for HOT-NIV vs. 1.4 months [IQR 0.5–3.9] for HOT) and reduced the likelihood of occurrence of the primary endpoint – readmission or death within 12 months – by ca. 50% (HR 0.49 [95% CI 0.31–0.77, $p = 0.002$]). The number needed to treat to avoid one readmission or death in this specific population was 6. Adjunction of NIV to HOT appears therefore useful in non-obese, non-apneic COPD who remain hypercapnic 2–4 weeks after an AEHRF episode.

For COPD patients in a stable clinical condition (more than 4 weeks after an AEHRF), a German and Austrian multicentric prospective RCT compared 102 patients treated by NIV (FEV₁: 26 ± 11% predicted, BMI 24.8 kg/m², PaCO₂: 58.5 ± 6 mm Hg [7.8 ± 0.8 kPa]) versus 93 on usual care (FEV₁: 27 ± 9% predicted, BMI 24.5 kg/m², PaCO₂: 57.7 ± 5.2 mm Hg [7.7 ± 0.7 kPa]) [96]. Inclusion criteria were: having a PaCO₂ of at least 7 kPa (52.5 mm Hg), and a pH >7.35 before randomization. They were followed for 12 months. High-intensity NIV was adjusted to reduce PaCO₂ below 48.7 mm Hg (6.5 kPa), or at least 20% lower than the baseline value. In this specific population, NIV significantly improved baseline PaCO₂, HRQL, and survival (mortality was 33% in the control group and 12% in the NIV group). It also reduced hospital admissions. The number needed to treat to avoid one death by NIV in this setting was 5.

Based on this evidence and closely following the most recent guidelines published by an ERS task force on NIV in COPD, the SIG suggests the following recommendations (all conditional) [98] (Fig. 7):

- Long-term NIV should be used in chronic stable hypercapnic patients (PaCO₂ >7 kPa [52.5 mm Hg]) with severe COPD¹.
- Long-term NIV should be implemented after an AEHRF only if hypercapnia (PaCO₂ >7 kPa [52.5 mm Hg]) persists 2–4 weeks after the acute episode.
- The potential benefit of long-term NIV for recurrent AERHF without persistent hypercapnia at 2–4 weeks remains undetermined.
- When implementing NIV in COPD patients with CHRF, settings should be adjusted to decrease PaCO₂ below 6.5 kPa (50 mm Hg) or reduce PaCO₂ levels by more than 20% of baseline level.
- When implementing NIV in COPD patients with CHRF, fixed PSV should be preferred to auto-titrating modes as first-choice mode.

NIV may also be considered as a component of palliative care and symptomatic treatment of dyspnea in end-stage COPD, irrespective of ABG and PFT [100]. Ventilator settings then aim to improve patient comfort, alleviate dyspnea, and decrease air-trapping and work of breathing.

Nota bene: Recent German national guidelines for NIV [10, 11] also include the following items as indications for NIV in COPD:

- Nocturnal hypercapnia with a PaCO₂ >55 mm Hg (7.3 kPa) irrespective of daytime PaCO₂.
- Mild nocturnal hypercapnia (46–50 mm Hg; 6.1–6.7 kPa) and an increase in PtcCO₂ ≥ 10 mm Hg (1.3 kPa) during sleep.

It is the opinion of the SIG that these indications are not sufficiently evidence-based to be recommended presently and require further evaluation.

2.2. Ventilator Settings

The use of PSV-ST and an IPAP of at least 18 cm H₂O is recommended [94], if tolerated. The use of a high BURR is a component of the “high intensity ventilation” strategy recommended by German guidelines [84, 85]. However, in a British 3-month randomized trial of “high pressure and high BURR” (IPAP 29 cm H₂O, BURR: resting respiratory rate – 2) versus “high pressure and low BURR (BURR: 6/min)” in 12 severe hypercapnic COPD, the high BURR component did not provide any additional benefit on ABG, nocturnal PtcCO₂, or average daily use of NIV, raising a doubt as to the necessity of a high BURR [86]. Short rise times (Fig. 2, top; 100–150 ms) are suggested to improve patient comfort and decrease work of breathing. Cycling criterion (Fig. 3, top) should be set at a high percentage of PIF, to allow time for expiration. As previously mentioned, several German studies have emphasized the benefit of high levels of pressure support (“high intensity NIV”) on PFT, symptoms, and correction of ABG [84–86]. Values of pressure support provided in the above-mentioned studies [96, 97, 99], as well as those reported in patients treated in Switzerland [4, 24], are in an intermediate zone with a satisfactory control of ABG (see online supplement; i.e., IPAP values of 18–25 cm H₂O). Values of PEEPi reported in stable severe COPD are in the 4–6 cm range [101, 102]. For patients with very severe airway obstruction, marked hyperinflation or hypercapnia, higher values of PEEPi must be anticipated and EPAP values titrated accordingly (i.e., up to 10 cm H₂O).

¹The ERS task force suggests a threshold PaCO₂ level of 6.7 kPa (50 mm Hg).

Because of the high proportion of patients with associated OSA among COPD recovering from an AEHRF [83], respiratory polygraphy or polysomnography with PtcCO₂ monitoring are recommended in these patients, and/or titration of EPAP considering the possibility of associated OSA.

2.3. Obstructive Lung Diseases Other Than COPD

CHRF related to diffuse bronchiectasis (cystic fibrosis [CF]-related and non-CF related). There are no RCTs of long-term NIV for bronchiectases, whether CF-related or not. Diffuse bronchiectases are recognized as a historical indication for long-term ventilation [103]. Use of NIV in diffuse bronchiectases is however associated with a poor prognosis [104, 105]. Uncontrolled data suggest that NIV may reduce symptoms and hospital admissions in CHRF-related to bronchiectasis [106–108]. In both CF-related and non-CF-related bronchiectasis, NIV may be used as a bridge to transplantation [109], and/or as an adjunct to airway clearance techniques and exercise training. For CF patients, 2 Cochrane reviews mention a short-term benefit of NIV on airway clearance and ABG in uncontrolled studies but are inconclusive as to the impact on survival [110, 111].

Severe bronchiolitis obliterans as manifestation of pulmonary graft versus host disease after stem cell transplantation or as chronic lung allograft dysfunction after lung transplantation may lead to CHRF and require NIV, either as a palliative treatment or as a bridge to transplantation. For these indications, no formal recommendations can be established, and the decision of implementing NIV must be taken by expert centers within a multidisciplinary management.

NIV may also be indicated as an adjunct to pulmonary rehabilitation in severe COPD, either during exercise training, or at night [112–117] (see section on special situations, 7.2).

3. Obesity-Hypoventilation Syndrome

3.1. General Comments

OHS is defined as the association of obesity (BMI ≥ 30 kg/m²), and daytime hypercapnia (PaCO₂ ≥ 45 mm Hg [6.0 kPa]), in the absence of any other restrictive or obstructive respiratory condition associated with alveolar hypoventilation [118]. OSA is present in 80–90% of cases and must therefore systematically be sought for as soon as clinically feasible. In the obese population, hypercapnia is associated with a worse prognosis (higher mortality,

higher rate of hospital readmission) [119]. NIV improves ABG, quality of sleep, and reduces risk of hospital readmission [120, 121].

Recent RCTs have clarified the respective roles of NIV and CPAP in OHS [63, 122–125]. The most important data come from the Spanish multicentric Pickwick study and from Australian RCTs. In 2008, Piper et al. [123] randomized 36 moderately hypercapnic OHS patients to PSV versus CPAP: after 3 months there was no significant difference between groups as to improvement in ABG, HCO₃, compliance, Epworth Sleepiness Scale (ESS), or HRQoL. However, patients with a daytime PaCO₂ > 55 mm Hg (7.3 kPa) and those with a nocturnal increase in PtcCO₂ or important nocturnal hypoxemia had been excluded from this trial.

A short-term RCT showed that NIV improved ABG and SRBD in OHS [126]. It also improved respiratory drive [127].

The Pickwick study randomized 86 OHS patients (mean PaCO₂ 49 mm Hg [6.5 kPa]) *without* severe OSA to NIV (volume-assured PSV) versus usual care [124]. After 2 months, NIV was superior to usual care for control of PaCO₂, HCO₃, daytime sleepiness, and HRQoL.

The same multicentric Spanish group randomized 221 patients with OHS (BMI: 44 ± 7 kg/m²; mean PaCO₂: 50 mm Hg [6.7 kPa]) and severe OSA in 3 groups: NIV, CPAP, and usual care [63]. After 2 months, NIV provided a marginal benefit when compared to CPAP in terms of PaCO₂ and HCO₃, while both NIV and CPAP were superior to usual care. 6 min walking distance and FEV₁ improved only in the NIV group. A substantial proportion of stable patients with OHS and OSA normalized their ABG (PaCO₂) when treated by CPAP alone and benefit was related to compliance.

An important contribution was the Australian study by Howard et al. [122]. These authors randomized 57 patients with OHS (mean age: 54 years, mean BMI: 54.9 kg/m²; PaCO₂: 59.6 ± 13.8 mm Hg [7.9 ± 1.8 kPa]; AHI: 82 ± 45 /h) to CPAP versus PSV: there was no difference in treatment failure (i.e., non-resolution or progression of hypercapnia) after 3 months. The most recent data from the Spanish Sleep Network group provide results of a long-term follow-up of 204 patients with OHS and severe OSA (average BMI: 43 kg/m²; baseline PaCO₂: 60 mm Hg [8 kPa]; AHI: 68/h) followed for a median of 5 years, randomized to volume-assured PSV versus CPAP: there was no difference between groups in terms of correction of ABG, number of hospitalization days or admissions, cardiovascular events, systemic blood pressure, or survival

Fig. 8. Noninvasive ventilation (NIV) in obesity-hypoventilation syndrome. Suggested algorithm. PSV, bi-level positive pressure ventilation; OSAHS, obstructive sleep apnea hypopnea syndrome; AHI, apnea-hypopnea index. See text for explanation.

[125]. Therefore, it appears clearly that NIV is not always mandatory in stable OHS with associated severe OSA, and that these patients warrant a trial of CPAP. A recent consensus statement has been published by the American Thoracic Society [128].

Based on this evidence, the SIG suggests the following recommendations (Fig. 8):

- For all OHS patients with an AEHRF, NIV is the recommended therapeutic option.
- Within 3 months of an AEHRF attributed to OHS, a native sleep study should be considered. In the presence of severe OSA, a trial of CPAP is appropriate. In case of mild/moderate or no OSA, pursuit of NIV is recommended.
- For stable patients, when ABG confirm the clinical suspicion of OHS, a sleep study is performed. An initial trial of CPAP is recommended if severe OSA is present (Fig. 8).
- For stable patients on long-term NIV for OHS, a switch to CPAP may be considered after documentation of presence of severe OSA.

In case of major weight loss (e.g., after successful bariatric surgery), the indication for CPAP or NIV must be reevaluated: in some cases (but not all) nocturnal positive

pressure treatment may be discontinued [129, 130]. It is mandatory that these patients be monitored on a regular basis (e.g., yearly) because of the possibility of partial or complete failure of bariatric surgery over time, with recurrence of OHS/OSA [131, 132].

As mentioned in the general comments, OHS patients are frequently comorbid, and management of comorbidities, screening for concomitant heart disease, integration in a weight loss program and/or orientation towards bariatric surgery, and rehabilitation are all important components of the management of these patients [133–136].

3.2. Ventilator Settings and Persistent Hypoxemia

The American Association of Sleep Medicine (AASM) and several other groups recommend the systematic use of PSG (polysomnography) for titration of NIV in OHS [137]. This is however not realistic in most countries, because of the restricted availability of PSG and, sometimes, the lack of expertise of sleep centers in NIV titration [138]. The SIG does not consider PSG as mandatory for titration of NIV. Titration of NIV with PSG may reduce patient-ventilator asynchrony but does not impact on quality of sleep, ABG, or somnolence [139]. PSG or polygraphy are however mandatory for diagnosing and quantifying associated OSA. Use of transcutaneous capnogra-

phy, whenever available, allows simultaneous assessment of the severity of nocturnal hypoventilation.

Once on positive pressure ventilation, a reasonable agreement between PSG and ventilator software determination of residual respiratory events has been documented in OHS (although in a limited number of subjects, and with devices from only one manufacturer) and thus, in clinical practice, ODI and ventilator software AHI can be used to control ventilator settings in combination with arterial blood gas analyses [66, 140, 141]. If ODI and AHI provided by ventilator software provide discordant results, a polygraphy or PSG may be contributive to a better documentation of residual respiratory events. Relying on ventilator-provided AHI alone is not recommended: nocturnal pulse oximetry should be combined with analysis of ventilator software [66].

Default devices for OHS are PSV ventilators. Although some groups use an “S” mode as a default option [123], the SIG recommends an S/T mode (spontaneous/timed), with a BURR close to spontaneous RR or slightly above. Use of a spontaneous (S) mode in OHS may increase occurrence of central apneas or hypopneas [142]. Conversely, a high BURR is associated with a better control of both central and obstructive residual events [142]. Some groups recommend PCV in severe OHS.

EPAP must be titrated to:

- control associated sleep-disordered breathing,
- improve V/Q relationships and nocturnal SpO₂, and
- compensate for auto-PEEP which is also reported in OHS (due to closure of peripheral airways, reduced FRC and increased closing volume) [143–147].

Rise time should be preferably in the 150–250 ms range. Cycling criterion should favor a prolonged inspiratory pressurization to improve the V/Q ratio and thus oxygenation (i.e., low percentage of PIF; Fig. 3, bottom).

Persistent hypoxemia under NIV is an adverse prognostic sign [148]. Therefore, pressure support aims to control not only daytime PaCO₂ but also nocturnal PtcCO₂ and SpO₂. Levels of EPAP and IPAP should be increased as much as tolerated before adding oxygen on the ventilator circuit. If PtcCO₂ is controlled, as well as AHI, but SpO₂ remains low, addition of oxygen on ventilator circuit may be considered [149]. There is no evidence that this impacts on outcome, but it does not affect PaCO₂ and optimizing nocturnal SpO₂ is a goal of NIV in all indications, mainly as a prevention of pulmonary hypertension and cor pulmonale [149]. Worsening of hypoxemia under NIV related to right to left shunt through a patent foramen ovale has been reported [150]. Conversely, NIV, when effective on ABG and nocturnal

SpO₂, has a positive impact on pulmonary hypertension and LVEF [151].

For patients already familiar with CPAP (failures of CPAP), or patients diagnosed in a stable clinical state, initiating NIV on an outpatient basis is feasible and currently performed routinely by many centers or private practitioners [4].

Persistence of obstructive events may result from either inappropriate settings (too low EPAP) or from the use of facial versus nasal masks [25, 152]. Several reports have documented that, for CPAP and NIV, facial masks may increase upper airway resistance by exerting a pressure on the mandibula, and thus compromise upper airway permeability. If obstructive events persist despite maximal EPAP tolerated and use of a nasal mask, increasing BURR has been shown to have a favorable impact on residual obstructive events [142].

The probability of daytime hypercapnia in OSA patients increases with BMI [153, 154]. However, there is no established classification of the severity of OHS according to BMI. A classification of severity of OHS has been suggested based on daytime levels of PaCO₂ in clinically stable patients (46–50 mm Hg [6.1–6.7 kPa]: mild; 51–55 mm Hg [6.8–7.3 kPa]: moderate; ≥56 mm Hg [7.5 kPa]: severe) [155]. In this retrospective study, the probability of controlling daytime PaCO₂ with CPAP decreased as severity of OHS increased. There was no mention however of whether failure of PSV could be predicted according to severity of daytime hypercapnia. Pragmatically, although not formally established, probability of failure of PSV appears higher in super obese subjects (defined as having a BMI ≥50 kg/m²). In this case, PCV or volumetric ventilation with PEEP may be required. Auto-adjusting PSV modes have not been shown to be superior to PSV-ST in “super-obese” subjects [33].

4. Restrictive Respiratory Diseases Other Than Obesity-Hypoventilation and NMD

Restrictive respiratory diseases (RLD) can be subdivided according to the major underlying physio-pathological disorder:

- RLD related to predominantly CWD, for example: kyphoscoliosis or other major chest wall deformities, ankylosing spondylitis, sequelae of chest trauma, or major chest surgery.
- RLD related to mixed diseases, for example: sequelae of collapse therapy – including thoracoplasty – for tuberculosis (presently mainly of historical interest).

- RLD related to predominantly parenchymal diseases: end-stage interstitial lung diseases (e.g., sarcoidosis, usual interstitial pneumonitis, hypersensitivity pneumonitis, pneumoconiosis), lung cancer (primary or metastatic) with or without lymphangitic carcinomatosis.

These entities lead to:

- A decrease in compliance of the respiratory system.
- An increased work of breathing, and impaired respiratory mechanics (geometric changes with a negative impact on respiratory muscle function) in the case of CWD.
- A variable impact on gas exchange, with, in the case of end-stage parenchymal diseases, frequently severe hypoxemia.
- In some cases, a decrease in ventilatory response to CO₂ [156].

There are no published RCTs for most of the disease groups mentioned above. Indication for NIV is based on observational studies [15, 157] showing a positive impact of NIV on HRQoL, hospital admissions, prevention of respiratory failure, endurance performance, and pulmonary hemodynamics [157–167].

CWD is a recognized indication for NIV: the natural history of the disease, depending on the severity of the chest wall deformity, is a progression towards CHRF with dyspnea on exertion, then resting dyspnea, hypoxemia (related to V/Q mismatch and zones of atelectasis), and pulmonary hypertension leading to cor pulmonale [168]. Nocturnal hypoventilation precedes daytime hypercapnia, can be detected by PtcCO₂, and is a prognostic factor for requirement of NIV within the following year [166]. NIV has been shown to be superior to LTOT in CWD, and is associated with an improved survival [169, 170]. Other studies have shown improvements in ABG, PFT, and HRQoL. There have been no new recommendations since the 1999 ACCP expert-based consensus statement [15].

The SIG recommends initiating long-term NIV for restrictive lung diseases in the presence of symptoms of hypercapnia (fatigue, dyspnea, morning headaches...) and at least one of the following physiological criteria:

Daytime hypercapnia (PaCO₂ ≥ 45 mm Hg [6 kPa])

Nocturnal hypoventilation according to AASM criteria, defined by Berry et al. [77]:

- *PtcCO₂ ≥ 55 mm Hg (7.3 kPa) for more than 10 min or*
- *An increase in PtcCO₂ ≥ 10 mm Hg (1.3 kPa) compared to awake supine value to a value exceeding 50 mm Hg (6.7 kPa) for more than 10 min.*

Nota bene. The criterion “SpO₂ < 88% for more than 5 min on nocturnal pulse-oximetry” mentioned in the 1999 consensus statement has been deleted, because of its lack of specificity, and the increasing availability of PtcCO₂ recordings.

4.1. Ventilator Settings

PSV in an S/T mode is the default approach. Values of EPAP are low, unless OSA is associated. Rise time should be preferably in the 150–250 ms range. Cycling criterion should be set to a low percentage of PIF (Fig. 3, bottom) to counteract the rapid decrease in inspiratory flow secondary to diminished chest compliance. Illustrative settings are provided in the online supplementary material.

Severe decreases in chest wall and/or parenchymal compliance may require high levels of pressure support over time, and use of PCV or volume-cycled devices as CRF progresses must be considered. In some cases, if quality of life is preserved, invasive ventilation may be considered.

Pulmonary rehabilitation has been reported as an efficient adjunct to long-term NIV in CWD [171].

5. Neuromuscular Disorders

5.1. General Comments and Caveats

- Neuromuscular disorders are a very heterogeneous group of diseases, with a variable prognosis (see Table 4 for most frequent indications for NIV in NMD). Each NMD has its own “agenda” as to the timing of the expected progression towards CHRF. Furthermore, within each NMD, this “agenda” is variable from case to case. Follow-up before NIV must be adapted accordingly.
- Dyspnea, and daytime hypercapnia are late events in the evolution of most NMD. Classical signs of respiratory failure such as tachypnea, recruitment of accessory muscles, or “tirage” may be masked by the underlying neuromuscular impairment. NIV must be implemented if possible *before* occurrence of daytime hypercapnia to prevent acute episodes of hypercapnic failure.
- Many NMD have systemic implications (cardiologic, digestive, endocrinologic, orthopedic...), and regular assessment by a *multidisciplinary expert team* is important. The frequency of follow-up consultations depends on the underlying disorder. Multidisciplinary management has been shown to im-

Table 4. Most frequent neuromuscular disorders associated with chronic alveolar hypoventilation

Myopathies and muscular dystrophies:
– Duchenne’s muscular dystrophy and Becker’s muscular dystrophy
– Myotonic muscular dystrophy (Steinert’s diseases)
– Limb girdle muscular dystrophy
– Congenital muscular dystrophies
– Metabolic myopathies (e.g., McArdle, Pompe, mitochondrial myopathies)
– Inflammatory myopathies (e.g., polymyositis/dermatomyositis)
Diseases of the muscular endplate
– Myasthenia gravis
– Paraneoplastic syndromes (e.g., Lambert-Eaton syndrome)
Motoneuron disorders
– Motoneuron diseases (e.g., Amyotrophic lateral sclerosis, Spinal muscular atrophies (type I–IV))
– Poliomyelitis and post-poliomyelitis syndrome
Diseases of brain stem and/or pyramidal tract
– Congenital or acquired central hypoventilation (Ondine’s syndrome)
– Traumatic spinal cord lesions
– Arnold-Chiari malformation and associated conditions
– Multiple sclerosis
Polyneuropathies
– Post-ICU critical illness polyneuropathy and myopathy
– Inflammatory neuropathies (e.g., Guillain-Barré)
– Phrenic neuropathies
– Other axonal neuropathies (toxic or paraneoplastic)

This list does not provide *all* possible neuromuscular indications for NIV.

prove prognosis per se in motoneuron diseases [172–174]. Advanced care planning should be a component of multidisciplinary management in all NMD, and especially in rapidly progressive disorders such as ALS.

- Treating NMD patients with NIV has socioeconomic implications and represents a high burden on families and caregivers. It is part of the management of these patients to ensure that they receive appropriate support by experienced social workers, that requests for devices such as (electric) wheel chairs, or communication devices are made in a timely fashion, and that home support is ensured so as to relieve the burden on families. The authors underline that management and home support of NMD patients should be improved in Switzerland and that appropriate funding should be provided and assured.

- Many NMD become clinically apparent in childhood or at adolescence, and patients and their families often have a multidisciplinary management follow-up by a pediatric team. Progressive and coordinated transition to the adult multidisciplinary disease management team must be carefully planned.
- In ALS, multidisciplinary management is associated with optimized timing of NIV. Even selected patients with bulbar dysfunction can derive benefit from NIV [175].
- Most of the evidence concerning NIV in NMD is based on observational studies [3, 104, 105, 165], albeit for ALS, for which an RCT with a small number of participants clearly showed that NIV improved HRQoL and survival in non-bulbar patients [176]. The fact that HRQoL does not deteriorate in patients with Duchenne muscular dystrophy after initiation of NIV was also demonstrated by Kohler et al. [177].

5.2. Follow-Up before Implementing NIV

- For all patients with NMD and a probability of evolution towards hypercapnic respiratory failure, a regular follow-up is mandatory and should include clinical assessment, targeted medical history, spirometry, vital capacity sitting and supine, sniff nasal inspiratory pressure *and* maximal inspiratory pressure, cough peak flow, nocturnal pulse oximetry (or whenever possible, nocturnal PtcCO₂), and daytime ABG. Nocturnal hypoventilation is predictive of requirement for NIV within the following months [166].
- Criteria proposed as threshold levels for implementing NIV are variable according to the underlying disease. Also, agreement between different criteria is often moderate or poor. Most tests used for follow-up of respiratory function are collaboration-dependent; their course over time may differ from one test to another [178, 179]. Bulbar dysfunction may also impair reproducibility of respiratory function tests. *A panel of functional tests performed at regular intervals is therefore preferable to appreciate the degree of respiratory muscle impairment* [20, 180].
- Frequency of follow-up depends on the underlying disorder and its expected progression (usually between 3 months and 1 year).

The SIG considers as clinical indications for NIV in NMD the following items:

- Control of symptoms related to respiratory muscle weakness and/or sleep-related hypoventilation or SRBD are per se an indication for NIV (e.g., morning headaches and fatigue, orthopnea, resting dyspnea, severe recruitment of accessory muscles, unexplained weight loss), even in the absence of daytime hypercapnia [181–183].
- Presence of sleep-disordered breathing (especially OSA) represents an increase in work of breathing, irrespective of symptoms, and NIV (because these patients will progress to CHRF) or CPAP should be considered.

Any one of the following are physiological indications for NIV in NMD:

- Daytime hypercapnia ($\text{PaCO}_2 \geq 45 \text{ mm Hg}$ [6 kPa]) or
- Daytime normocapnia with nocturnal hypoventilation measured by PtcCO_2 according to AASM criteria (because of a high risk of rapid progression to daytime hypercapnia):
 $\text{PtcCO}_2 \geq 55 \text{ mm Hg}$ (7.3 kPa) for more than 10 min or
An increase in $\text{PtcCO}_2 \geq 10 \text{ mm Hg}$ (1.3 kPa) compared to awake supine value to a value exceeding 50 mm Hg (6.7 kPa) for more than 10 min.
- Vital capacity <50% of predicted or sniff nasal inspiratory pressure/maximal inspiratory pressure <40 cm H_2O , especially in rapidly progressive NMD.

Comment: Metabolic alkalosis should suggest the possibility of nocturnal hypoventilation and should lead to specific investigations. Also, prevalence of nocturnal hypoventilation varies widely according to definitions provided [78].

5.3. Ventilator Settings

- Some expert centers consider that NIV in NMD should be preferentially performed with volume-cycled devices, and with alarms, because of the risk of prolonged central sleep apnea or hypopnea, and for the security of the patient. Over the past decades, however, there has been a drift towards the use of PSV in S/T mode as default approach, at least as an initial modality (see section on highly dependent patients). Life support devices provide all the necessary alarms for patient safety.
- In most NMD, compliance of the respiratory system is marginally affected if chest wall deformity is not severe and pressure support levels are generally low.

- EPAP values may become a factor of discomfort when respiratory muscles are severely affected, and should be kept at minimal values in the absence of SRBD.
- Inspiratory trigger settings may require adjustment (increase in sensitivity) as disease progresses.
- An “S” mode is *not* recommended as standard setting, but can be used for special situations (i.e., eating with NIV, mouthpiece ventilation). An S/T mode with a BURR close or slightly above spontaneous RR is standard. The authors suggest to titrate BURR so as to minimize percentage of cycles triggered by the patient, and thus minimize residual work of breathing (i.e., “capture” the patients’ spontaneous RR).
- Rise time is set according to patient comfort, usually 150–250 ms. Higher values will significantly impinge on pressurization and should be used only exceptionally.
- It is an unexplained but frequent observation that patients with NMD are often more comfortable when slightly hyperventilated.
- Patient-ventilator asynchrony may occur in NMD (mostly in motoneuron disease) as a consequence of paradoxical movements of the vocal cords which may compromise the efficacy of ventilation [184]. Strategies to adapt ventilator settings have been proposed [25].
- Adjunction of oxygen is seldom required in the absence of any underlying lung disorder.
- For many NMD, use of NIV will become necessary outside of the home (i.e., adapted to an electric wheel chair), requiring a built-in battery with prolonged autonomy; also, use of interfaces such as mouthpieces may be useful: in this case, multimodal ventilators with performant built-in batteries and specific modes for mouthpiece ventilation are recommended [185]. When dependence to NIV reaches 16 h/day, having a back-up “life support-type” ventilator (i.e., a second device) is mandatory.

5.4. Interfaces in NMD

- Mouthpiece ventilation must be considered in very dependent patients to facilitate speech and social contacts, and to provide ventilator support while on the move (electric wheelchair). Several ventilators presently provide a “mouthpiece” mode which facilitates implementation of mouthpiece ventilation [185].
- Use of nasal pillows may also increase comfort during the daytime.

- Although there is a theoretical risk of aspiration when using facial masks in patients who cannot easily remove their interface, in clinical practice, facial masks are often the only way to control the frequently occurring mouth leaks, and are therefore used regularly (56% of NMD cases in the GLS study) [4]. Auxiliary means to facilitate the removal of the mask by the patient (e.g., hand strap) should be then considered. The alternative – use of a chin strap and nasal mask – is a possible option.
- In 24-h NIV dependency, a common approach is to use an oro-nasal/face mask during sleep and nasal pillows or a nasal mask during daytime.

5.5. Mechanical Insufflation/Exsufflation in NMD

Assessment of *ability to cough* must be performed systematically in all patients with NMD, and, if necessary, specific treatment must be implemented.

MIE devices provide a mechanical assistance for patients with an impaired ability to cough. These devices can be used with a facial mask, a mouthpiece, or a tracheostomy cannula, in children or adults. With appropriate teaching, these devices can be used by non-professional caregivers, or sometimes by the patient alone. Training is usually provided at home or at the hospital/specialized center by experienced physiotherapists or respiratory therapists/nurses. Illustrative video supports can be easily downloaded from the internet, although they do not replace appropriate individualized training.

Basically, MIE simulates the physiological cough process by providing 3 phases: (a) an insufflation phase to increase lung capacity as close as possible to TLC and benefit from the elastic recoil of the respiratory system; (b) an inspiratory plateau which may be provided manually (to improve synchronization) or automated (to facilitate home treatment by non-professional caregivers); (c) an exsufflation phase: a negative pressure is applied to the airways, which, combined with the elastic recoil pressure of the respiratory system, generates an expiratory flow which mobilizes secretions. Use of MIE can be combined with manually assisted cough techniques to improve efficacy [186, 187].

Nota bene. These recommendations will not describe techniques such as “glosso-pharyngeal breathing,” “air-stacking,” manually assisted coughing or other techniques to assist airway clearance. These techniques are part of the standard management of secretions and airway clearance in severe NMD [188, 189].

The SIG suggests the following recommendations for implementing the use of MIE (Fig. 9):

In all cases, clinical assessment is mandatory, and MIE devices may be considered as necessary irrespective of cough peak flow values.

The indication for MIE is based on the inability to clear secretions in an effective manner (clinical assessment) and measurements of the cough peak flow:

270 L/min: cough is probably efficient.

160–270 L/min: cough may be inefficient; it is mandatory to instruct the patient and caregivers on appropriate assisted cough techniques and, if they fail, to evaluate MIE devices.

<160 L/min: spontaneous cough is most probably inefficient to clear secretions from the airways, and the use of assisted cough techniques is mandatory. If they fail or are not feasible, MIE devices are necessary.

Use of MIE should be encouraged on an outpatient basis in all patients with NMD, a decreased cough peak flow, and difficulties to clear their airways from secretions with assisted cough techniques.

Training at home can be provided to caregivers and/or unexperienced healthcare workers by experienced physiotherapists or respiratory therapists. Repeated interventions for caregiver education may be necessary.

MIE settings. A recent report from an expert center (Royal Brompton Hospital, UK) provided average settings for MIE from 181 patients with NMD (130 adults, 51 children; 156 with NIV, 8 with a tracheostomy) as well as an algorithm for establishing MIE settings [190]. Values reported for adults were (median; IQR): 28 cm H₂O (25–30) for insufflation; –35 cm H₂O (–32; –40) for exsufflation; TI: 1.5 s (1.3–1.8); expiratory time: 2.0 s (1.5–2.4); pause: 1.5 s (1.3–2.0). Most patients used automated modes. Rarely, higher pressures may be required, when compliance of the respiratory system is markedly decreased (severe obesity, kyphoscoliosis), or in patients with a tracheostomy and a small canula, to overcome the additional airway resistance. Initiation is usually performed with lower insufflation pressures (15–20 cm H₂O). Pressures are then increased gradually beginning with exsufflation pressures [186, 187].

In motoneuron disease, paradoxical movements of the vocal cords and closure of upper airways (adduction of aryepiglottic folds, retroflex movement of the epiglottis, closure of hypopharynx, backward movement of the tongue) during MIE may compromise its efficacy and require adapting (decreasing) pressure levels and using a manual mode [191]. This does not only occur in bulbar

Fig. 9. Threshold levels for cough peak expiratory flow for implementing mechanical insufflation/exsufflation. This must be combined with clinical evaluation of cough efficacy.

onset patients. Susceptibility to MIE settings may also change over time. Inspiratory values are critical: in patients with motoneuron disease, higher cough peak flow values were obtained using insufflation pressures of 30 versus 40 cm H₂O [192]. Insufflation values may have to be decreased to 15 cm H₂O, with asymmetrical settings for insufflation and exsufflation (i.e., maintaining higher exsufflation than insufflation pressures) [191]. Decreasing insufflation pressures and flow combined with longer TIs may improve upper airway stability in these cases [193]. Triggering insufflation by the patient may also be effective to reduce closure of the upper airway. In experienced centers, these events can be detected by transnasal video laryngoscopy [184, 191, 193, 194].

Patient information. An application for cell phones and tablets (Apple or Android) developed by the Geneva CeSLA team is available as freeware for ALS patients and caregivers (CeSLApp).

6. Sleep-Related Breathing Disorders

6.1. General Comments

For most SRBD, positive pressure treatment is provided either with CPAP, or adaptive servo-ventilation (ASV) [5, 195, 196].

SRBD is the 1st indication for NIV in the French AN-TADIR observatory (www.antadir.org; ASV not included). Conversely, in the GLS study, patients with SRBD represent only 9% of patients under NIV.

6.2. Indications

The SIG recommends NIV for SRBD in the following situations:

- *OSA and failure of CPAP because of persistence of abnormal AHI/RDI/ODI, and/or poor tolerance and/or requirement of high pressures to control respiratory events. In this indication, NIV can most often be implemented on an outpatient basis.*
- *Normo- or hypocapnic central sleep apnea. This includes Cheyne-Stokes breathing and other forms of periodic breathing. When CSA are either idiopathic, induced by medication (e.g., opiates), or associated with neurological disorders (most often cerebrovascular diseases), NIV using PSV-ST can be considered after failure of CPAP or ASV. ASV is slightly superior to PSV in opiate-induced CSA [197] and is more appropriate to avoid hyperventilating these patients, which could aggravate the underlying SRBD.*
- *Hypercapnic central sleep apnea. This group includes CSA induced by medication (e.g., opiates) or associated with neurodegenerative diseases. In these settings, titration of NIV must be monitored by respiratory polygraphy or polysomnography, with transcutaneous capnography. In certain NMD (namely ALS), care must be taken to avoid or control paradoxical movements of vocal cords [25].*

In case of cardiac dysfunction (LVEF ≤45%) and Cheyne-Stokes breathing, ASV is contra-indicated. Alternative treatments must be discussed after optimiza-

tion of medical treatment of chronic heart failure (fixed pressure nCPAP, oxygen...) [198]. There is, however, no evidence against the use of NIV in this setting in hypercapnic patients.

7. Special Situations

7.1. The Highly Dependent Patient

A small group of patients under long-term NIV will become severely or totally dependent of their ventilator support. In the recent GLS survey, 2% of all NIV patients used their ventilator more than 16 h/day. These patients have most often advanced NMD (ALS, Duchenne muscular dystrophy...), very severe COPD or other causes of tetraplegia (post traumatic or not).

The SIG group raises several issues of concern.

(1) *Security*. Because an interruption of ventilator support for a few minutes or hours may in some cases be fatal, having at home one *spare* ventilator ready to use, plugged and charged, with the same settings, is mandatory. Both ventilators must belong to the “Life support” category of home ventilators.

The French guidelines published by the “Haute Autorité de Santé” (November 2012) recommend that all patients requiring the use of their ventilator for more than 16 h/day be equipped with two “life support” home ventilators. This is also the case in the German national guidelines for HMV [12] and is the usual practice of British and Belgian centers.

The SIG authors recommend that a second (back-up) ventilator should be provided when daily use of NIV exceeds 16 h/day because:

- *Minor changes in respiratory status (i.e., lower or upper respiratory tract infection) can lead to total dependence in a matter of hours or days.*
- *Not having a second device available in this context can be a major risk in areas where rapid intervention at home is not available.*
- *Conversely, a second device is the best way to avoid unnecessary admissions to an emergency ward for purely technical reasons.*
- *Evolution towards a complete dependence on NIV is a matter of weeks or, at most, months in these patients.*

Importantly, the second ventilator is contributive to improving the autonomy of the patient since it can be used for mouthpiece ventilation and/or on an electric wheelchair and/or in a separate part of the home.

(2) *Autonomy*. As mentioned above, use of a second ventilator allows having a device for an electric wheelchair, and/or for use with a mouthpiece, and/or for travelling. This can also be required in a home with stairs.

(3) *Appropriate home support*. For *highly dependent* patients, the NIV team must ensure that appropriate support is provided to caregivers, and that adaptations of home environment are organized when necessary. These patients usually require 24/24-h support 7 days/week, and financial support as well as trained care givers must be made available, irrespective of the financial situation of the patient’s family. Although this is the case in most EU countries, the financing of this support is not guaranteed in Switzerland, and funding must often be sought for via patient associations, or private foundations (e.g., Pro Infirmis).

In case of a medical or technical problem, a hotline must be available for the patient’s care givers and advance care directives must have been discussed and clarified.

For patients travelling abroad – which is possible for severely dependent NMD patients for instance if appropriately planned – temporary allocation of an additional back-up ventilator may increase level of security when confronted to another health system and different health-care providers. Local reference “hotline” numbers must be provided in case of technical problems.

7.2. NIV and Rehabilitation

NIV has 2 documented indications in pulmonary rehabilitation. The first is to increase tolerance to exertion in severely limited patients (i.e., during or just after an ICU stay for acute exacerbation, or as a first step for a severely limited and bed-ridden patient). In this indication, NIV may allow bed-ridden subjects to walk, or perform exercises on cycloergometers, thus potentially accelerating their recovery, although this is not formally demonstrated [115, 164, 199–205]. This approach can also be provided at home for patients performing their exercises under supervision.

The second indication is as an add-on treatment, e.g. nocturnal NIV during a rehabilitation program, with benefits documented in hypercapnic COPD and ILD patients [206, 207].

NIV during exercise should be adapted by experienced chest therapists/physiotherapists according to patient comfort. Increasing pressure support is usually required, as well as EPAP to decrease dynamic hyperinflation in severe COPD [208]. Rise time and TI_{MIN} must be adapted to the patient’s increase in respiratory rate.

Table 5. Comparison of invasive and non-invasive long-term home ventilation

	Invasive ventilation	Non-invasive ventilation
Advantages	<ul style="list-style-type: none"> – Suctioning of lower airway secretions facilitated – Cuff inflation provides some protection against aspiration of secretions and foreign material – Application of higher airway pressure feasible – Quantitative monitoring of ventilation reliable – Advanced alarm functions available 	<ul style="list-style-type: none"> – Non-invasive – Convenient initiation and withdrawal, intermittent use – Swallowing and speech not impaired – Near-normal life when not on NIV, less stigmatization – Independent usage
Disadvantages	<ul style="list-style-type: none"> – Invasive procedure required – Risk of tracheomalacia, tracheal stenosis, and bleeding – Stigmatization of patient in daily life – Speech and swallowing may be impaired – Higher risk of lower airway infection – Limited care facilities available 	<ul style="list-style-type: none"> – Cooperation required – Mask leaks common, in particular with high pressure support – Risk of skin damage/pressure ulcers – In patients requiring continuous or near-continuous ventilatory support, eating/drinking is problematic – Airways are not protected
Suggested indications	<ul style="list-style-type: none"> – Severe, life-threatening ventilatory failure – Failure of NIV – Continuous ventilatory support (20 h/day) needed and not feasible via NIV – Reliable alarms needed (life support) – Severe bulbar dysfunction – Fixed upper airway obstruction – Severe hypersalivation and swallowing difficulties 	<ul style="list-style-type: none"> – Intermittent, non-life-sustaining support needed – Sleep-disordered breathing

7.3. NIV and Palliative Care

NIV is a possible option in palliative care, for example, for patients with advanced oncologic disorders, progressive respiratory failure related to end-stage interstitial lung disease, or post stem-cell or solid organ bronchiolitis obliterans [209]. End-stage interstitial lung disease is often associated with severe dyspnea, and a major increase in work of breathing. Treatment, its timing, and settings are primarily symptom-based, and implementation must be performed by therapists experienced in NIV. Rate of failure of symptom control may be high [210, 211]. NIV must aim to improve symptom control, but not prolong unnecessary suffering or discomfort. Deciding when to withdraw NIV should be discussed with the patient and his/her close relatives before implementing NIV or invasive ventilation. In diseases leading to impaired communication (such as ALS), and potentially to a locked-in syndrome, it is particularly important to clarify beforehand when ventilator support should be interrupted [212, 213].

Alternative treatments under clinical evaluation are high-flow, humidified oxygen, or CPAP.

7.4. Invasive HMV

7.4.1. Invasive Ventilation in Switzerland and Other Countries

Long-term positive pressure ventilation via tracheostomy (TPPV) remains a valuable option for a subgroup

of specifically selected patients. In a European survey, patients treated with TPPV represented 13% of the population on long-term mechanical ventilation [82], with a wide variability from country to country. In a British study of all-cause mortality of 1,210 patients under HMV over a 10-year period, patients using TPPV represented 12% of the deceased [214]. A similar proportion of TPPV in HMV has been reported in Canada [215]. Detailed data of non-hospitalized patients on TPPV in Switzerland are not available but figures are probably much lower. Among 3,498 patients who started home ventilation between 2016 and 2019, 48 (1.4%) patients were under TPPV (annual report, Schweizerischer Verband der Krankenkassen; SVK). In the GLS Study, 11 of the 500 patients under HMV (2.2%) were under TPPV, a number which has remained stable over the past 20 years [4]. Patients with spinal cord injuries or chronic NMD who are 24h-ventilator-dependent represent the most important subpopulation on TPPV.

7.4.2. Conditions in Which TPPV Is Used

TPPV may be initiated following invasive mechanical ventilation in the ICU due to acute or acute-on-chronic respiratory failure with subsequent weaning failure. In NMD with bulbar dysfunction or massive secretions, elective tracheotomy may be an option. In some centers, TPPV is routinely initiated when patients with NMD

such as Duchenne's muscular dystrophy (DMD) become ventilator dependent. However, 24-h NIV is also feasible and convenient for many DMD and other neuromuscular patients and is standard practice in many centers [216–219]. The availability of NIV together with MIE (Cough assist) is likely to reduce the need for invasive ventilation.

In rapidly progressing NMD such as motor neuron disease with bulbar dysfunction, the question of TPPV arises often and requires careful consideration [213]. The final decision is the patient's, and a non-biased complete information to the patient and his/her caregivers should be provided well in advance. Items to be discussed include: expected burden for caregivers in case of 24-h home care, limited availability of nursing home beds, specific complications, possibility and modalities of withdrawal from invasive ventilation and end-of-life care. Some institutions have published their concept of TPPV in motor neuron disease [213]. Recommendations and patient decisions are influenced by personal, cultural, and ethical aspects, and informed decisions in terms of prognostic expectations as well as end-of-life-care should be made individually.

There is no robust evidence to support recommendations on indications of TPPV. However, Table 5 lists some points to be considered.

7.4.3. Consequences of TPPV

TPPV creates a major burden for caregivers in Switzerland because options for long-term care of ventilator-dependent tracheotomized patients outside the hospital are limited and financial support for qualified help at home is often insufficient. Healthcare costs for patients with chronic respiratory failure are far higher for invasive than for non-invasive ventilation [220]. Management of patients on invasive ventilation usually requires 24-h care. This burden is often left to the close family who has to be trained in tracheostomy care, airway clearance, and emergencies. Specific, formal lay person training programs exist for instance in France and Germany but not in Switzerland. Furthermore, long-term care institutions for this population are almost inexistent in Switzerland. However, for slowly progressive neuromuscular and chest wall disease, the Mathilde Escher Heim in Zurich is an example of a specialized care center where a large cohort of patients with muscular dystrophy or other NMD live and/or attend school and pursue a professional activity.

Quality of life on long-term TPPV, implemented after careful preparation, may be good in patients with muscular dystrophy or CWD [177, 221, 222]. It may however be

severely impaired in patients with unscheduled tracheostomy after weaning failure in the ICU, for instance in COPD [223]. To improve quality of life, mobility is an important aspect for patients on TPPV. Therefore, 2 ventilators, of which one is portable or attached to an electro-wheelchair should be available. These ventilators must have built-in batteries that allow a safe mobility for several hours.

TPPV is associated with the risk of specific complications such as life-threatening – although rare – tracheal bleeding, ventilator-associated pneumonia, obstructive mucus plugging or tracheal granuloma formation and stenosis that may increase morbidity and mortality compared to NIV [224–226]. Data on outcomes of long-term tracheostomy ventilation come from cohort studies but have not been systematically analyzed and compared to NIV in a conclusive way [214, 215, 227, 228].

7.4.4. Practical Aspects

In general, TPPV patients and patients with an anticipated ventilator dependency should be managed in a specialized tertiary center by a multidisciplinary team. A specific knowledge of circuits, cannulas, humidifiers, ventilators, speech functions, and TPPV-associated complications is mandatory. An overview on the topic has been published recently and is summarized here [23].

TPPV can be delivered via surgical tracheotomy or percutaneous dilatational tracheostomy (usually performed in the ICU). Both techniques have specific complications, that is, risk of instability during cannula exchange in the early phase and bleeding in case of percutaneous dilatational tracheostomy or an oversized lumen in case of surgical tracheotomy.

Cannula and cuff. Different cannula types are available (length, angle, diameter, flexible vs. rigid, with and without cuff, fenestrated vs. closed) [189]. The choice of the right tracheal cannula size and length is important to avoid leakage and damage to the trachea. Regular change of the outer tracheal cannula should be performed, at least initially, by an experienced team. Typical intervals are 6–8 weeks but depend on the amount of secretions and other aspects (e.g., local pain). A replacement tracheal cannula of the same size and of a smaller size should always be available. Inner cannulas are often changed several times a day. An inflated cuff reduces the risk of aspiration but cannot reliably protect from this complication. Conversely, an inflated cuff can cause pressure ulcers and compromise swallowing. It is recommended to apply a low cuff pressure that is periodically monitored, and to avoid permanent cuff inflation.

A tracheotomy affects swallowing and speech. *In the initiation phase of TPPV, intensive training of laryngeal function and speech training while the cuff is deflated are important.* Some patients with preserved bulbar function may not need a cuffed tracheal cannula or require TPPV with an inflated cuff only during sleep.

When a cuff is inflated and seals the trachea properly, secretions cannot enter the lower airways. However, if patients cannot swallow secretions, they may accumulate above the cuff balloon. This results in desensitization of the cough reflex in the upper airway and larynx. A deflated cuff allows airflow towards the upper airway for speaking and coughing. It is important that the tracheal cannula chosen is thin enough to allow air passage to the upper airway while the cuff is deflated, especially during use of a one-way speech valve (Passy Muir® or similar valve). Application of a speech valve while the cuff is inflated can be life-threatening since only an inward flow is possible.

If a fenestrated cannula is used, both a closed and a fenestrated inner cannula must be available. When using the fenestrated inner cannula and a deflated cuff together with a speech valve, phonation is facilitated due to air flowing around the cannula and through the fenestration towards the larynx.

Circuits. Different circuits (single- vs. double-limb) are available for TPPV. Both a single-limb non-vented circuit with an exhalation valve (active circuit) or, less commonly, an intentional leak connector (passive circuit) and a double-limb circuit with separate inspiratory and expiratory limbs are available for TPPV [218]. Separate in- and expiratory limbs allow a reliable quantitative monitoring of VT, minute ventilation, and leaks. However, a single-limb circuit is easier to handle.

Ventilators. Different life-support ventilators are available for invasive HMV (online suppl. Table S1). As previously mentioned (section 7.1), 2 ventilators are mandatory for security reasons in highly dependent patients. Different settings for day- and night-time may be used. Pressure-controlled ventilation (PCV) or volume controlled ventilation are more commonly used than PSV in TPPV [214]. A target-volume might be set in addition to pressure modes, but advantages of this have not been demonstrated so far. Specific alarms are available for invasive ventilation with life-support ventilators. Noteworthy is the fact that VT and VE cannot be accurately measured when cuff is deflated (unintentional leak through upper airway): this impairs alarm functions.

Humidification. Heated humidification is standard in invasive HMV during the night to avoid desiccation of

the airways and thus bleeding and obstruction with mucus plugs. However, humidification is seldom feasible in patients who are mobile in a wheel-chair: in this situation heat- and moisture-exchanging filters are sufficient in most cases.

Suctioning and mechanical in-/exsufflation. Suctioning of the upper and lower airways is routinely performed in TPPV. Deep suctioning should be limited because of the risk of mucosal lesions. Chest physiotherapy (assisted cough techniques) and mechanical in-/exsufflation with a Cough assist are important adjunctive measures to mobilize peripheral secretions towards the central airways.

7.4.5. Special Considerations in Spinal Cord Injuries

Spinal cord injuries affect the respiratory system through several mechanisms [229–233]:

- Loss of control of respiratory muscles, even at low spinal cord injury levels (affecting pelvic and abdominal muscles).
- Decreased chest wall compliance, which can progress after the initial lesion.
- Altered central respiratory control and negative impact of frequently used CNS suppressants (antispasmodic and pain-relieving medications).
- Diaphragm dysfunction (e.g., “paradoxical orthopnea”), because of abdominal distention (chronic constipation and intestinal dysautonomy) or increased intra-abdominal pressure (spasticity) [234, 235].
- Bronchial hyperreactivity in injuries above TH 6, due to sympathetic roots disconnection [236, 237].
- SRBD [238, 239].
- Impaired clearance of airway secretions.

Requirement for ventilatory support. For lesions at a level of C3 or above, initial invasive mechanical ventilation is almost invariably required. A change to electrostimulation of the diaphragm (direct stimulation of the motor points of the diaphragm or by phrenic nerve stimulation) has, in selected patients, some advantages in comparison to conventional mechanical ventilation even for long-term use [240, 241].

For lesions at C3 or below, the requirement for continued ventilatory support varies from case to case, and nocturnal NIV may be an option.

SRBD in spinal cord injury. Prevalence of SRBD in spinal cord injury is 4–5 times that of the general population; it is higher in tetraplegics (60–90%) than in paraplegics (55%) [242–244]. OSA impairs HRQoL in tetraplegic subjects as well as cognitive function [245, 246]. Additional risk factors for SRBD in tetraplegics include narrowing of the upper airways due to surgical proce-

dures to stabilize the spine, hyperplasia of neck muscles, and loss of the stretching effect on upper airways due to decreased lung volumes [247, 248].

CPAP is the treatment of choice for para- and tetraplegic patients with OSA and no sign of hypoventilation. In higher spinal cord injury level, low pressures often suffice. Higher pressures can lead to poor tolerance, especially in the presence of expiratory muscle weakness. In these cases, PSV therapy is an option.

Central sleep apnea syndromes, often due to medications, are not uncommon and are treated according to methods used in other patients with this disorder (CPAP, ASV, PSV).

Because chest wall compliance may decrease over time in tetraplegics and patients with high-level thoracic lesions, thus increasing work of breathing, alveolar hypoventilation may develop after the initial injury, and will appear initially during the night. Therefore, in the long-term follow-up of patients with high-level spinal cord injury, the risk of nocturnal hypoventilation must be considered. If nocturnal hypoventilation (with or without daytime hypoventilation) is confirmed, NIV is indicated usually with PSV devices in both PSV and PCV modes.

In the presence of SRBD and suspicion of nocturnal hypoventilation, which are often combined, further workup should include a polygraphic study which is easier to undertake than a PSG in a sleep laboratory (sleep labs are seldom equipped and trained for spinal cord injury patients), combined with continuous PtcCO₂ recording [249].

Specific aspects related to NIV in spinal cord injury. NIV in high-level tetraplegia is generally possible if used during the night and partially during the day. However, 24-h non-invasive ventilation in tetraplegics is rare.

PCV and PSV modes are both used during the night. There are no studies comparing PSV to PCV modes in this population. Patient acceptance may be better with PCV modes especially in tetraplegics. If PSV modes are used, a backup frequency is mandatory because of frequent central apneas. Mouthpiece ventilation on demand or nasal prongs can be used during mobilization on a wheelchair.

Careful choice of masks, and appropriate setting of alarms are crucial, together with a specific training of all caregivers. Safety of patients with limited or no capacity to handle their mask by themselves in routine or in an emergency must be anticipated. Therefore, hospitalizations are usually required to initiate NIV.

Importantly, pressure support requirements may change over time due to changes in chest mechanics: pa-

tients with a rather recent spinal cord injury often need lower pressures than patients with a stiffened thoracic cage years after the initial lesion.

In all patients with spinal cord injury and ventilatory support, a regular follow-up is required, initially at 3- to 6-month intervals, and subsequently once or twice a year.

As in all ventilator-dependent patients, a second device is always necessary if daily requirement for ventilatory support is ≥ 16 h. This is also the case if the patient needs a ventilatory support during daytime while using an electric wheelchair, to enhance mobility and autonomy. Indeed, ventilator settings in a sitting position may differ from those used supine, and repeated dismantling and reinstalling of ventilators on a wheelchair may cause a safety problem. In this case, a built-in battery with a sufficient autonomy is necessary ("life support device") and a supplementary battery may be required.

7.4.6. Management of Airway Secretions and Use of MIE (see also section 5.5)

The success of any ventilatory support for all para- and tetraplegic patients depends on efficient coughing. Two components are important: (1) to reach a maximal inspiratory capacity before coughing, and (2) to maximize peak cough flow. The first target can be reached by techniques such as continuous training of the remaining inspiratory muscles, air stacking, glossopharyngeal breathing, insufflation with a resuscitation bag, or use of a MIE device (or NIV if a MIE mode is available) [250]. The second goal can be reached by self-assisted cough techniques while supine or sitting in a wheelchair, assisted cough techniques administered by caregivers, or with MIE. A target peak cough flow of >270 L/min should be reached for cough to be efficient.

8. Transition between Acute Care and Home (or Long-Term Institution)

Success of long-term home NIV (or NIV in a health care institution) depends on appropriate preparation and timing of the transition, anticipation of present and future requirements in terms of environment and training of caregivers, and anticipation of disease progression. Providing appropriate psychological, social, and financial support for the family and caregivers is also of major importance.

A multidisciplinary assessment and preparation of the transition to home care is necessary to include all the possible aspects of patient management in his/her new envi-

Table 6. Goals for transition from hospital to home care (or institution)

- Ventilator settings must provide the best possible control of alveolar hypoventilation (monitored by PtcCO₂ and/or ABG)
- Patient is stabilized, and *comfortable* with his/her home ventilator
- The patient or his/her caregivers are autonomous in putting on and taking off the mask and in maintenance of the equipment (cleaning, use of the humidifier, etc.)
- Necessary home care is organized (intervention of nurses, other healthcare workers [HCWs], chest therapists, physical therapists, technical control of ventilator and other devices)
- Home caregivers have been trained for all technical tasks, and written support is provided
- Professional support can be reached 24 h/day and 7 days/week to provide appropriate guidance
- When required, backup equipment is immediately available on site
- Financial aspects are covered, and patient and/or his/her family are not exposed to a burden they cannot face

Home healthcare providers must ensure that:

- they have been extensively informed of all relevant items regarding patient and treatment before he/she is transferred
- all caregivers (GP, pulmonologist, chest therapist, etc..) are identified, and that all necessary contact information is in their possession
- they have enough qualified/trained HCWs to provide a high level of care with substitutes in case of leave absences, sickness leaves, etc.
- they offer a hotline for technical support 24/24 h 7/7 days
- they will provide regular feedback to the pulmonologist in charge, as well as results of tests agreed upon with the treating pulmonologist (i.e., pulse oximetry, data from ventilator software, transcutaneous capnography, etc.)
- HCWs within the Health Care Provider organization receive regular and structured training in the field of management of chronic respiratory failure

ronment. Practical teaching should be started early and performed throughout the hospital stay for caregivers and level of competence and understanding should be regularly assessed by the hospital team. A checklist may be useful to ensure coverage of all necessary tasks to be performed at home.

As previously mentioned, for invasive ventilation, in neighboring countries, short certifying training sessions are organized covering all aspects of respiratory care. Availability of this type of training should be encouraged in Switzerland for patients on invasive ventilation and/or for severely dependent patients.

When a transfer is planned to another long-term medical institution, training of the healthcare workers of this institution must be initiated as early as possible. Contacts

must be encouraged to create bonds between the patient and his/her future caregivers. This is also important to decrease the level of stress and anxiety of the patient, his/her close relatives, and among healthcare workers. Finally, time is needed to ensure acquisition of the necessary competences.

Evaluating the adequacy and ergonomics of the home environment, and, if necessary, performing the required changes, must be organized with the social workers, ergo-therapists and physical therapists/physiotherapists.

Goals for transition to home care are summarized in Table 6.

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Conflict of Interest Statement

J.-P.J., F.M., E.I.S., M.P., K.E.B., D.A., A.-K.B., A.G., W.K., A.O., S.O., J.R., O.D.S., M.S. W.S., C.U., and G.G. have no conflict of interest regarding the manuscript.

Author Contributions

J.-P.J., F.M., E.I.S., M.P., K.B., D.A., A.-K.B., A.G., W.K., A.O., S.O., J.R., O.D.S., M.S., W.S., C.U., G.G. have provided substantial contributions to the conception or design of the work and/or or the acquisition, analysis, or interpretation of data for the work *and* contributed to drafting the work and/or revising it critically for important intellectual content *and* have given final approval of 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.

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