Practical Guide to Management of Long-Term Noninvasive Ventilation for Adults With Chronic Neuromuscular Disease

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Introduction
    Goals of Long-Term Ventilatory Support
Part I. Devices
    Devices for Home Ventilatory Support
    The Breathing Cycle
    Modes of Assisted Ventilation
    Monitoring Assisted Patient Triggered Ventilation
Part II. Management
    Indications for Initiation of Nocturnal Noninvasive Ventilation
    Initiation Phase
    Maintenance Phase
    Daytime Ventilation
    Tracheostomy
    End-of-Life Respiratory Care
Part III. Troubleshooting and Problem Solving
    Face Mask Discomfort
    Excessive Air Leak
    Excessive Airway Secretions
    Upper-Airway Resistance
    Patient-Ventilator Asynchrony
    Aerophagia
Conclusion

Recent technological advances in respiratory support and monitoring have dramatically enhanced the utility of long-term noninvasive ventilation (NIV). Improved quality of life and prolonged survival have been demonstrated for several common chronic neuromuscular diseases. Many adults with progressive neuromuscular respiratory disease can now comfortably maintain normal ventilation at home to near total respiratory muscle paralysis without needing a tracheostomy. However, current practice in many communities falls short of that potential. Mastery of the new technology calls for detailed awareness of the respiratory cycle; expert knowledge of mechanical devices, facial interfaces, and quantitative monitoring tools for home ventilation; and a willingness to stay current in a rapidly expanding body of clinical research. The depth and breadth of the expertise required to manage home assisted ventilation has given rise to a new focused medical subspecialty in chronic respiratory failure at the interface between pulmonology, critical care, and sleep medicine. For clinicians seeking pragmatic "how to" guidance, this primer presents a comprehensive, physician-directed management approach to long-term NIV of adults with chronic neuromuscular respiratory disease. Bi-level devices, portable ventilators, ventilation modalities, terminology, and monitoring strategies are reviewed in detail. Building on that knowledge base, we present a step-by-step guide to initiation, refinement, and maintenance of home NIV tailored to patient-centered goals of therapy. The quantitative approach recommended incorporates routine monitoring of home ventilation using technologies

that have only recently become widely available including cloud-based device telemonitoring and non-invasive measurements of blood gases. Strategies for troubleshooting and problem solving are included. *Key words: chronic respiratory failure; respiratory insufficiency; noninvasive ventilation; assisted ventilation; home ventilation; telemonitoring; neuromuscular disease; amyotrophic lateral sclerosis; muscular dystrophy.* [Respir Care 0;0(0):1–●. © 2023 Daedalus Enterprises]

Introduction

Almost from the beginning of modern mechanical ventilation, severely impaired children and adults with chronic neuromuscular disease have been living at home with the benefit of respiratory support devices designed for use outside of hospitals.[1,2] The tank and cuirass shell respirators, rocking beds, and piston-driven positive-pressure ventilators that emerged for long-term home use during the polio epidemics of the mid-20th century set the stage for recent explosive growth in the use of home assisted ventilation.[3] Noninvasive ventilation (NIV) now predominates and is widely used to sustain children and adults with neuromuscular respiratory failure. Prolonged survival and improvements in quality of life have been demonstrated for several common neuromuscular diseases.[4-8] Many patients referred early to experts in home ventilation can now be managed noninvasively as weakness progresses to near total respiratory muscle paralysis.[9-11] Accumulating evidence favors aggressive efforts to optimize home ventilation;[12-16] however, professional education and training lag the technical advances in this emerging field, creating an unmet need for up-to-date educational resources.[17-20]

The purpose of this clinical guide is to present a quantitative, physician-directed strategy for managing long-term NIV. We focus on chronic diseases of the respiratory pump that impair breathing including congenital, inflammatory, and degenerative nerve or muscle diseases; traumatic quadriplegia; isolated bilateral diaphragm paralysis; and severe thoracic skeletal disorders such as idiopathic kyphoscoliosis. The primer is intended to function as a comprehensive study guide for clinicians new to management of chronic respiratory failure and as a technical reference resource for experienced clinicians. Our primary target audience is

United States pulmonologists, sleep medicine specialists, respiratory therapists, pulmonary advanced practice providers, and other clinicians seeking to master long-term ventilation for people 16 y of age and older.

We cover goals of ventilatory support, ventilatory devices, monitoring tools, indications for initiation of therapy, a stepwise approach to refining initial device setup, long-term management, and troubleshooting. The quantitative strategy presented incorporates routine application of noninvasive monitoring of gas exchange and cloud-based device telemonitoring data. Though vitally important to comprehensive management of chronic respiratory failure, this guide does not cover mechanical insufflation-exsufflation and other techniques for airway clearance.

Goals of Long-Term Ventilatory Support

Quantitative management of any chronic disease requires a delineation of the goals of care. Yet, we have found only one published consensus statement on goals for long-term assisted ventilation. In 2020, members of the Swiss Society of Pulmonology suggested the following 4 goals: (1) clinical improvement and reduction in daytime P_{aCO_2}, (2) mean nocturnal $S_{pO_2} > 90\% > 90\%$ of recording time without residual S_{pO_2} oscillations, (3) at least 4 h/night of use without discomfort, and (4) correction of nocturnal hypoventilation.[21] We propose a patient-centered realignment of those goals.

Enable Restful, Restorative Sleep. Sleep disturbance is an early common manifestation of neuromuscular respiratory disease.[22-24] Sleep fragmentation, depression of arousal mechanisms, obstructive and central apneas, alterations in sleep architecture, and intermittent or continuous hypoventilation give rise to frequent nighttime awakenings, unrefreshing sleep, daytime fatigue, morning headaches, and daytime hypersomnolence. These manifestations of respiratory muscle weakness can be ameliorated or reversed by optimal nocturnal NIV.[24]

Relieve Breathlessness. People with chronic neuromuscular respiratory disease almost universally experience uncomfortable breathing.[25-27] For adults with a chronic neuromuscular disease, even mild, intermittent breathlessness is anxiety provoking and debilitating.[27] Combined as needed with other palliative modalities, efficacious assisted ventilation can be highly effective in reducing breathlessness experienced by patients suffering from respiratory muscle weakness, thereby considerably improving quality of life.

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Normalize Respiratory Gas Exchange Night and Day. The benefits of normalizing P_{aO_2} for people with chronic hypoxemia are supported by large-scale, randomized clinical trials and are widely accepted.[28] No randomized clinical trial has demonstrated the benefit of normalizing P_{aCO_2} (< 45 mm Hg) relative to a more permissive target in the management of chronic neuromuscular respiratory failure. However, information is accumulating on the protean adverse biological effects of elevated or reduced P_{aCO_2} in animal models and humans.[16,29-36] In agreement with several current guidelines and statements,[21,37,38] we recommend titration of home assisted ventilation to normalize P_{aCO_2} as well as P_{aO_2} to the extent possible without necessitating excessive peak inspiratory pressures, breathing discomfort, or other trade-offs.

All 3 goals are achievable for many people with neuromuscular respiratory failure; however, trade-offs are sometimes necessary for those with a concomitant severe thoracic skeletal abnormality or lung disease that requires high peak inspiratory pressures to overcome high airway resistance or low respiratory system compliance. Prolonged survival is not included as a universal goal to respect individual preferences for continuation of life support in advanced neuromuscular disease.

Part I. Devices

Devices for Home Ventilatory Support

The appropriate application of NIV in the home setting requires application of 4 interrelated devices: a facial interface, a circuit, a ventilatory support device, and in most instances a heated humidifier.

Ventilatory Devices. Broadly considered, 3 types of ventilatory support devices are used for home NIV: (1) *bi-level devices* known to the United States Centers for Medicare and Medicaid Services (CMS) as *respiratory assist devices* (RADs) (Medicare Healthcare Common Procedure Coding System [HCPCS] codes E0470, E0471), (2) *portable ventilators* (E0466), and (3) *multimodality respiratory devices* (E0467). The capabilities and limitations of these devices are compared in Table 1.

Bi-level devices evolved from CPAP machines to improve treatment of sleep apnea and are designed for tabletop use. These machines support pressure targeted bi-level ventilation, typically delivered through the same single-limb circuit that is used for CPAP therapy. Current versions transmit use and performance data via Bluetooth to a dedicated application on the patient's cellular telephone or tablet. Some models can also be configured to communicate via intermittent cellular transmission to a cloud-based server, thereby enabling clinicians to review detailed performance data and modify settings remotely. Bi-level machines are not

life-support devices. Advanced models are suitable for nocturnal NIV of selected patients with neuromuscular respiratory disease who do not ordinarily need ventilatory support when out of bed (Fig. 1).

Portable ventilators derive from hospital ventilators and are configured to function as life-support devices. They include an internal battery for security and portable use, precision control over all components of the breathing cycle, a broad range of ventilatory modes and modifications, multiple presets, a large display screen, access to real-time monitoring of pressure and volume waveforms, and a full range of configurable alarm settings. In contrast to bi-level devices, portable ventilators are not authorized by the United States Food and Drug Administration for remote adjustment of settings or alarms. Home ventilators available for use in North America are illustrated in Figure 2.

The VOCSN multimodality Life System (Ventec Life Systems, Bothell, Washington) incorporates 5 respiratory treatment modalities (ventilation, oxygenation, cough assistance, suction, and nebulizer) into one device. VOCSN ventilators are fully portable when operated on an internal battery. At 8.2 kg for the base ventilator and more for the attachments needed to implement the several treatment modalities, VOCSN is heavier than single-modality devices (Table 1).

Facial Interfaces. Vented nasal and oronasal masks are used predominantly for home NIV. These masks incorporate open ports in the mask shell or an integrated swivel connector to create an intentional leak throughout the respiratory cycle. The leak ports flush exhaled carbon dioxide from the mask.

More than 200 vented face masks are commercially available today in a vast array of configurations.[39,40] Philips, ResMed, Fisher & Paykel, and Drive DeVilbiss frequently update a full range of positive airway pressure (PAP) face masks suitable for home NIV. Sleepnet, Circadiance, Airway Management, BleepSleep, and others make specialized facial interfaces that may be preferred by some people with challenging fit or comfort needs. Specialized mouthpieces are also available for diurnal NIV.

Circuits. With minor variations, 3 types of circuits are used to support home ventilation: dual-limb active circuits with expiratory valves, single-limb active circuits with expiratory valves, and single-limb passive leak circuits without expiratory valves. All these circuits can be used for NIV. However, most adults currently undergoing NIV at home for neuromuscular disease are supported using a single-limb passive circuit connected to a vented face mask or a mouthpiece. Lightweight, flexible, single-limb circuits exert less pull on face masks and pair well with home respiratory devices that provide flow compensation for variations in air leak at the

Table 1. Devices for Home Noninvasive Ventilation

	Advanced Bi-Level RADs HCPCS E0471	Portable Ventilators HCPCS E0466	Multifunction Ventilators HCPCS E0467
Functions	Patient triggered ventilation	Patient triggered ventilation	Patient triggered ventilation Supplemental oxygen Cough assist Suction Nebulizer
Examples	Philips DreamStation ResMed AirCurve	ResMed Astral Philips Trilogy Legacy and Evo Breas Vivo 45 Löwenstein LUISA	Ventec VOCSN
Device weight	1.2–3.0 kg	2.5–6.0 kg	8.2 kg
Power source	External outlet	External outlet Internal battery Optional external battery	External outlet Internal battery Optional external battery
Circuits	Single-limb passive Single-limb passive, heated	Single-limb passive Single-limb passive, heated	Proprietary valveless single-limb passive Proprietary single-limb passive, heated
Modes*	CPAP Spontaneous Spontaneous/Timed	CPAP Pressure support Spontaneous Spontaneous/Timed Timed (T) Pressure control	Bi-level Spontaneous (MPV only) Pressure Control CMV Volume Control CMV Pressure Control SIMV Volume Control SIMV
Modifications*	VAPS	VAPS Auto-EPAP MPV	Volume-targeted ventilation MPV
Presets	Single	Multiple	Multiple
P_{Imax}	25–30 cm H_2O	50–60 cm H_2O	40 cm H_2O > PEEP
Monitor Screen	Small	Large	Large
Data Transfer	SD Card Bluetooth Cellular modem	USB download Cellular modem	USB download
Remote Setting Changes	Yes	No	No
Alarms	Limited event detection Limited audible alarms on advanced models	Multiple configurable audible alarms	Multiple configurable audible alarms
Cost	$$	$$$$	$$$$$

*Manufacturers use proprietary terms for several ventilatory modes and modifications.
RAD = respiratory assist device
HCPCS = Healthcare Common Procedure Coding System (United States Centers for Medicare and Medicaid Services)
MPV = mouthpiece ventilation
SIMV = synchronized intermittent mandatory ventilation
VAPS = volume-assured pressure support
auto-EPAP = automated expiratory positive airway pressure
P_{Imax} = maximum inspiratory pressure
SD = secure digital
USB = universal serial bus

patient interface. Because exhaled air escapes directly from the interface, exhaled tidal volumes (V_T) and minute ventilation ($\dot{V}_E$) cannot be measured directly. Instead, they are estimated from dynamic flow measurements using proprietary algorithms.

Humidification Systems. Heated humidification of inspired air is considered mandatory for invasive ventilation to protect lower-airway mucosa from deleterious effects of breathing unconditioned air[41] and is recommended for PAP treatment of sleep apnea.[42] Limited research published to date has not shown a convincing physiological benefit of humidification for long-term NIV. Nevertheless, many people undergoing NIV report less irritation or obstruction of nasal passages and less mouth drying when breathing humidified air. Accordingly, practice guidelines issued by the American Association for Respiratory Care suggest heated humidification during NIV to improve comfort and adherence.[41]

Most bi-level devices incorporate a built-in humidifier. Most ventilators require a separate device to humidify
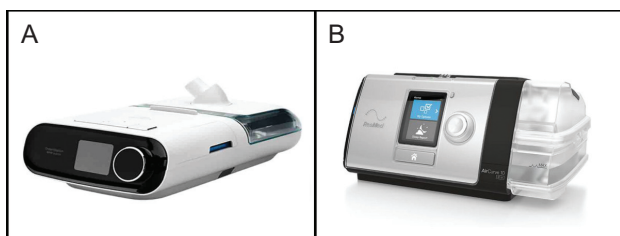
Fig. 1. Bi-level devices (RADS). A: Philips DreamStation BiPAP; B: ResMed AirCurve 10 ST-A.

inspired air. Passive heat and moisture exchangers are not recommended for NIV through a vented mask because humidified exhaled air escapes before passing through the exchanger. Instead, for stationery use of home ventilators, a separate humidification chamber filled with distilled water is placed midway along the tubing circuit and warmed by an electric hot plate to generate heated, humidified air. The percent saturation of water vapor at body temperature delivered to the patient can be increased by adding heated tubing to the circuit. Fisher & Paykel HC and MR series humidifiers are commonly used in the United States for home assisted ventilation (Fig. 3).

The Breathing Cycle

Advanced bi-level respiratory devices and all portable ventilators allow custom control of ventilator function during all phases of the breathing cycle (Fig. 4). Every setting must be adjusted correctly to assure comfortable, efficacious breathing.

Applied Pressure, Tidal Volume, and Rise Time. Positive-pressure ventilatory devices alternate applied pressure between 2 levels, an inspiratory PAP (IPAP) and an expiratory PAP (EPAP). Pressure support (PS) is the difference between IPAP and EPAP. If enabled, a specified backup breath rate determines the minimum number of breaths/min.

Both IPAP and EPAP can be set to a fixed value by the operator. In addition, advanced bi-level devices and home ventilators enable continuous machine-automated adjustment of IPAP within a preset range ($IPAP_{min}$/$IPAP_{max}$) to maintain a specified V_T (target V_T [Philips], or safety V_T [SV_T] or alveolar $\dot{V}_E$ [ResMed]). The rise setting specifies the time required after a breath is triggered for pressure to rise from EPAP to IPAP. As shown in Figure 4, V_T is proportional to the area under the flow-time curve determined by inspiratory flow, rise time, and the duration of inspiration.

Transition From Expiratory to Inspiratory Positive Pressure. Spontaneous breaths begin when a patient's inspiratory effort generates a change in the inspiratory flow exceeding the trigger set point. The device automatically initiates a mandatory breath if the breath-to-breath interval exceeds the interval determined by the preset backup rate (60 s/set rate).

On Philips devices, the trigger sensitivity can be set to Flow Trigger at a preset inspiratory flow or to either of 2 automated settings, Auto-Trak or Auto-Trak sensitivity. These latter settings automatically modify trigger and cycle algorithms with the goal of preserving patient-ventilator synchrony. Auto-track sensitivity was designed for people

Fig. 2. Portable ventilators. A: ResMed Astral; B: Philips Trilogy Legacy; C: Philips Trilogy Evo; D: Ventec V+Pro; E: Breas Vivo 45 LS; F: Löwenstein LUISA. The Ventec VC+Pro single modality critical care ventilator should not be confused with the 5-in-1 Ventec VOCSN multimodality life support system, which looks similar.
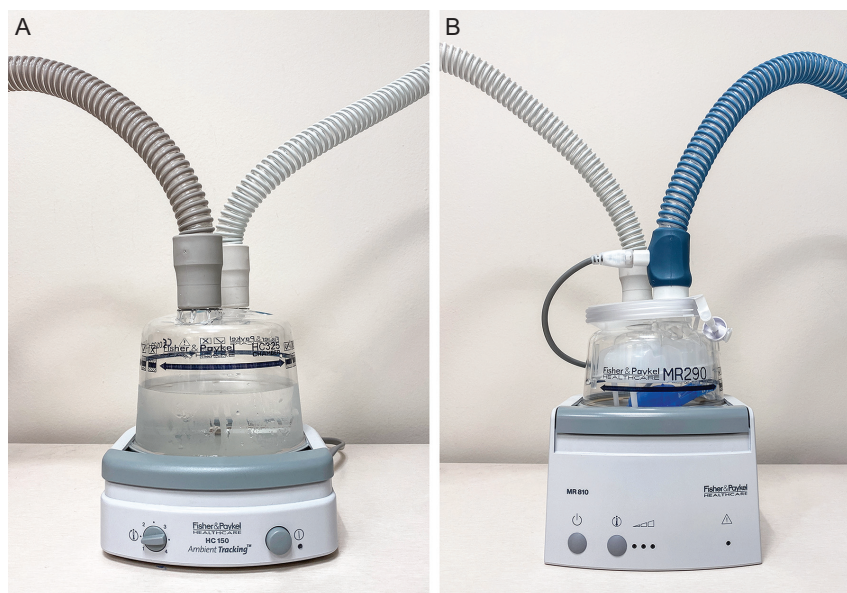
Fig. 3. External heated humidifiers. A: Fisher & Paykel HC150 humidifier paired with an HC325 water chamber; B: Fisher & Paykel MR810 humidifier paired with an MR290 water chamber, which includes heated tubing. The MR810 humidifier deployed with heated tubing delivers a higher fraction of saturated water vapor with higher relative humidity at body temperature. For bed-bound patients continuously dependent on ventilation, the MR290 water chamber can be filled continuously using a fill tube attached to a water reservoir bag hung above the device. The fill tube is shown here coiled on top of the water chamber.

with severe respiratory muscle weakness who generate minimal inspiratory effort during ventilatory support.

ResMed bi-level devices and ventilators offer 5 different flow sensitivity adjustments for trigger from Very Low to Very High. The higher the selected sensitivity, the smaller is the patient-generated inspiratory flow required to trigger inspiration. ResMed ventilators use flow triggering for single-limb passive circuits and pressure triggering for single-limb active circuits. Dual-limb circuits can use either flow or pressure triggering.

Transition From Inspiratory to Expiratory Positive Pressure. Cycling refers to the end of the inspiratory phase of a breath cycle. Cycling occurs when a predetermined inspiratory flow or time threshold is attained. Flow-cycled breaths end when the patient's inspiratory flow falls below the rate determined by the cycle setting expressed as a percent of maximum inspiratory flow. The higher the sensitivity selected (higher percentage of maximum inspiratory flow), the smaller is the reduction in inspiratory flow required to cycle to expiration and thus the shorter the respiratory time. Time-cycled breaths end when the duration of the inspiratory phase of the respiratory cycle reaches the preset inspiratory time (T_I). ResMed devices and Philips Trilogy Evo ventilators offer the option of a preset T_I window (T_I min/T_I max) to prevent either premature or delayed cycling.

Modes of Assisted Ventilation

The modes of ventilation determine how home ventilators control machine augmentation of patient respiratory effort. Various manufacturers implement these options differently and apply different proprietary terminology to describe them. This primer uses non-proprietary terminology whenever possible and, when necessary, the terminology employed by some home ventilator manufacturers.

All devices designed for home ventilation enable spontaneous (S) ventilation (PS with no backup breath rate). This mode is suitable for treatment of selected patients with sleep apnea, obesity hypoventilation, or chronic obstructive pulmonary disease. S mode is not recommended for adults with neuromuscular respiratory disease, many of whom are prone to irregular breathing patterns during sleep.[43-45]

Instead, advanced modes are appropriate for these patients such as *spontaneous/timed ventilation* (S/T), *pressure control* continuous mandatory ventilation (PC-CMV), or pressure control intermittent mandatory ventilation (PC-IMV).

Modifications to these two primary modes are available for special purposes. Volume-assured PS (VAPS), a type of adaptive pressure support, targets a preset V_T or alveolar $\dot{V}_E$ by automatically adjusting inspiratory pressure within a preset window. Automated expiratory PAP (auto-EPAP) automatically adjusts end-expiratory pressure within a preset window to overcome upper-airway resistance. Mouthpiece ventilation (MPV) offers specialized settings for patients who breathe through a mouthpiece instead of a face mask.

The available pressure modes and volume modifications are detailed in Table 2.
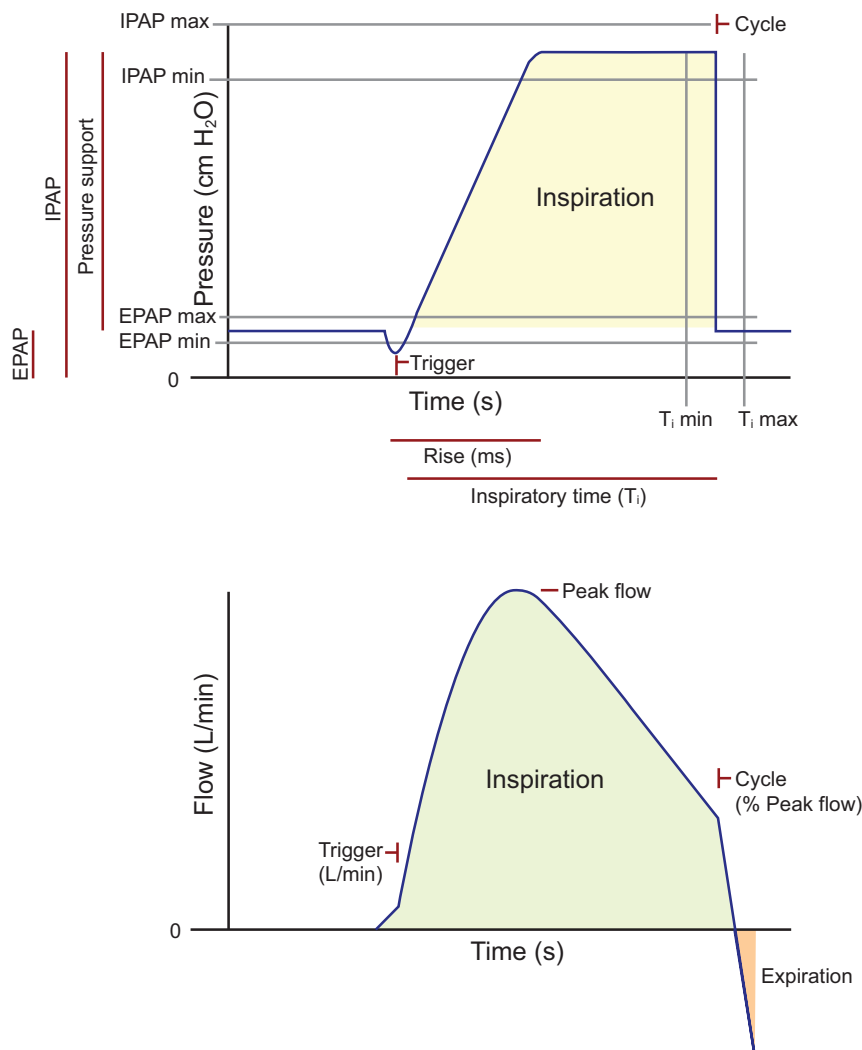
Fig. 4. Terminology describing components of a pressure assist inspiration delivered through a single-limb passive circuit. Tidal volume is proportional to the area under the flow-time curve shown here in green. IPAP = inspiratory positive airway pressure; EPAP = expiratory positive airway pressure.

Spontaneous Timed Mode. S/T mode applies a set backup breath rate to bi-level ventilation. All breaths above the set backup rate start and end in response to patient effort and are assisted to deliver a fixed, preset inspiratory and expiratory pressure. Mandatory breaths protect against episodes of slow or absent breathing by assuring machine-iniatiated breaths at the backup rate.

Pressure Control Mode. PC mode is the same as S/T mode ventilation except that all breaths are time cycled. PC ventilation is used for patients with severe respiratory muscle weakness who may not be able to sustain an inspiratory effort long enough to generate a satisfactory V_T.[46]

Modifications of Primary Modes. Reflecting a general lack of standardization in assisted ventilation terminology, some manufacturers refer to some modifications of

S/T and PC ventilation as separate modes. Care is required to navigate these differences.

Volume-Assured Pressure Support. With VAPS enabled, the machine automatically adjusts the applied inspiratory pressure within preset limits to maintain a preset target V_T or alveolar $\dot{V}_E$. The purpose is to maintain adequate ventilation in response to sudden or slow changes respiratory muscle strength or respiratory system mechanics that alter the relationship between pressure and volume.

On advanced Philips bi-level devices and ventilators, VAPS is implemented in either S/T or PC mode by setting a proprietary algorithm termed average VAPS (AVAPS). Pressure is automatically adjusted within a preset minimum and maximum window at a preset rate of change to maintain a preset target V_T. With AVAPS enabled in S/T mode, all spontaneous breaths are flow cycled and all mandatory

Table 2. Comparison of Recommended Modes and Settings for Noninvasive Ventilation

	S/T	PC	Adaptive pressure ventilation*	Adaptive pressure ventilation**	MPV
Flow	Continuous	Continuous	Continuous	Continuous	Inspiration only
Backup rate	Yes	Yes	Yes	Yes	Yes
Expiratory pressure	Fixed	Fixed	Fixed or automated	Fixed or automated	Zero
Inspiratory pressure	Preset fixed	Preset fixed	Varies within preset limits	Varies within preset limits	PC-MPV Varies for VC-MPV
V_T	Varies	Varies	Targeted	Varies	Varies
Backup rate	Fixed	Fixed	Fixed or automated	Automated	Zero
Alveolar $\dot{V}_E$	Varies	Varies	Varies	Targeted	Varies
Trigger and cycle	Spontaneous breaths: patient triggered, flow cycled	Spontaneous breaths: machine triggered time cycled	Trilogy legacy: same as S/T	Spontaneous breaths: patient triggered flow cycled	Patient triggered
	Mandatory breaths: machine triggered time cycled	Mandatory breaths: machine triggered time cycled	Trilogy Evo: configurable	Mandatory breaths: machine triggered time cycled	Patient or machine cycled
Best for	Stable mild to moderate respiratory muscle weakness	Stable severe respiratory muscle weakness	Increasing muscle weakness	Increasing muscle weakness	Daytime ventilation
			Variable respiratory system mechanics	Variable respiratory system mechanics	

* Philips devices.
** ResMed devices.
S/T = spontaneous/timed
PC = pressure control
AVAPS = average volume-assured pressure support
iVAPS = intelligent volume-assured pressure support
MPV = Mouthpiece ventilation
V_T = tidal volume
$\dot{V}_E$ = minute ventilation

breaths are time cycled. On Philips devices set to PC mode with AVAPS enabled, spontaneous as well as mandatory breaths end when the duration of inspiration reaches the preset T_I. When AVAPS is used, Philips ventilators allow adjustment of the maximum rate (from 1–5 cm H_2O per min) at which PS changes to achieve and maintain the target V_T (termed AVAPS rate on Trilogy Legacy ventilators and AVAPS speed on Trilogy Evo ventilators).

On ResMed ventilators (but not bi-level devices), a target V_T can be set in S/T or PC mode by specifying an SV_T. With SV_T enabled, ResMed ventilators automatically increase or decrease PS breath by breath in 0.2–2.0 cm H_2O increments within the preset min/max window to maintain the target V_T.

Using a proprietary algorithm, *intelligent VAPS (iVAPS)*, advanced ResMed bi-level devices and Astral ventilators enable the operator to target a specified alveolar $\dot{V}_E$ within a preset min/max pressure window. Alveolar $\dot{V}_E$ is automatically estimated by subtracting from total $\dot{V}_E$ an estimated value for dead-space $\dot{V}_E$ based on patient height.

The intelligent backup rate (iBR) feature of iVAPS automatically shifts the backup rate between either of 2 limits. The lower rate limit (backup rate) equals two thirds of the preset target breath rate. If spontaneous triggering falls below that rate, iBR resets the backup rate within several breaths to the target breath rate. A subsequent single spontaneous triggered breath resets the backup rate to two thirds of the target breath rate. The intent is to maximize spontaneous breathing while also protecting against central apneas or periodic breathing. iBR does not protect against acute or chronic hyperventilation resulting from a spontaneous respiratory rate that exceeds the set target rate.

Auto-EPAP. With VAPS enabled, home ventilators can be set to activate machine titration of EPAP (auto-EPAP) to maintain patency of the oropharyngeal airway at end expiration. When auto-EPAP is activated, IPAP$_{min}$ and IPAP$_{max}$ are replaced with a PS window (PS_{min}/PS_{max}) to preserve control of the inspiratory driving pressure as EPAP varies over time. Currently available bi-level devices do not offer this option.

On Philips ventilators, auto-EPAP is enabled by selection of AVAPS-AE (automated EPAP) ventilation. On Trilogy Legacy devices, AVAPS-AE resembles S/T mode in that all spontaneous breaths are flow cycled and all mandatory breaths are time cycled. Trilogy Evo ventilators offer two options for controlling T_I in AVAPS-AE ventilation that are not available on Trilogy Legacy devices.

When *PC breath* is enabled, the T_I setting applies to all spontaneous as well as mandatory breaths (like A/C-PC with AVAPS enabled). If *PC breath* is disabled, the T_I setting applies only to mandatory breaths (like S/T with AVAPS). Evo ventilators also enable the setting of a T_I window. This option is available through the "Advanced" tab on the Evo Prescription window.

AVAPS-AE mode also enables automated adjustment of the backup breath rate. Because the backup rate is adjusted based on the patient's spontaneous breath rate, we do not recommend this option for patients at risk of breathing at an undesirably slow rate during sleep.

ResMed Astral ventilators offer auto-EPAP in iVAPS mode. ResMed auto-EPAP automatically adjusts expiratory pressure within preset $EPAP_{min}$ and $EPAP_{max}$ limits in response to machine-detected obstruction of the upper airway.

Mouthpiece Ventilation. MPV substitutes a mouthpiece for a face mask to maximize the comfort and functional independence of selected people who regularly need assisted ventilation during the day. Device settings are adapted so that patients can control the rate and volume of assisted breaths by partly or completely sealing their lips around a mouthpiece during inhalation. Between breaths, flow is reduced to an undetectable rate. See the Daytime Ventilation section in Part II for additional information on MPV.

Monitoring Assisted Patient Triggered Ventilation

Our proposed goals of therapy provide a framework for assessing and monitoring NIV for people with neuromuscular disease. Recent technological advances have dramatically improved access to quantitative data on respiratory pump dysfunction and respiratory device performance.[47,48] We employ four primary monitoring modalities: respiratory symptom assessment, selected measures of pulmonary function, noninvasive measures of gas exchange, and respiratory device telemonitoring.

Respiratory Symptom Assessment. No monitoring modality is more important for NIV than assessing the patient's experience of breathing. People living with chronic neuromuscular disease may not spontaneously communicate symptoms attributable to respiratory muscle weakness or assisted ventilation because of impaired phonation or because they believe that such experiences are inevitable and inescapable in their situation. Accordingly, both before and after initiation of NIV, we routinely ask patients whether they are experiencing uncomfortable breathing or other potential manifestations of respiratory insufficiency including poor sleep quality, daytime hypersomnolence, and increasing fatigue toward the end of the day. An affirmative answer prompts further questioning. Note that comfortable breathing does not assure normal ventilation. Some people with severe neuromuscular disease may not experience breathlessness despite chronic hypercapnia because of a blunted respiratory drive.

The Severe Respiratory Insufficiency Questionnaire is used by clinical researchers to assess overall health-related quality of life for people undergoing assisted ventilation at home.[49] At least 3 questionnaire-based rating scales have been developed since 2018 to assess and score respiratory-related symptoms of motor neuron diseases prior to initiation of assisted ventilation.[50-52] These scales have not been validated for other neuromuscular diseases. The 11-item S^3-NIV Questionnaire scores relevant symptoms and ventilator-related adverse effects after onset of assisted ventilation[53] (Fig. 5). S^3-NIV was designed to support clinical research but can also be useful to guide selection of questions for clinical assessment.

Vital Capacity. Forced vital capacity (FVC) measured in an upright position is the best studied objective measure of the severity and rate of progression of respiratory muscle weakness.[54-57] Vital capacity (VC) is an integrative measure that reflects alterations in thoracic elastance as well as expiratory and inspiratory muscle strength. The slow VC (SVC) is increasingly used as an alternative to FVC because it allows a gentler expiratory effort and requires less lip and jaw strength to maintain a tight seal at the mouthpiece.[58] Because diaphragm weakness differentially reduces the supine VC, FVC or SVC is often also measured in this position to assess people with suspected or known respiratory muscle weakness. A difference $> -15\%$ between the sitting and supine VC strongly suggests diaphragm weakness.[59]

Measurements of VC can be performed in a pulmonary function laboratory, an out-patient office, or at home by patients using a personal spirometer.[60,61] Handheld "smart" spirometers such as the MIR Spirobank Smart (Medical International Research, New Berlin, Wisconsin) and the NuvoAir Air Next (NuvoAir, Boston, Massachusetts) spirometers (Fig. 6) can automatically transmit data to a patient's telephone or tablet for subsequent transmission to clinicians. With appropriate patient training, personal spirometers have proven feasible for home monitoring of VC.[62,63]

Spirometry should be performed with a nasal clip in place using a calibrated spirometer under the supervision of a qualified clinician.[64,65] For people who are unable to maintain a tight seal with the mouthpiece of a spirometer, an unvented oronasal mask used with manual resuscitator bags or a mouthpiece constructed with a flexible flange between the teeth and lips such as the ComFit rubber mouthpiece (SDI Diagnostics, Easton, Massachusetts) can be used to achieve an adequate pressure seal. Patients with advanced bulbar or respiratory muscle disease may not be able to perform a reproducible maximum expiration by any means.

	Always true	Mostly true	Sometimes true	Mostly untrue	Completely untrue	Score
1. I suffer from breathing problems when I eat.	0	1	2	3	4	
2. I often have a headache.	0	1	2	3	4	
3. I wake up at night with breathing difficulties.	0	1	2	3	4	
4. I am often short of breath .	0	1	2	3	4	
5. I have trouble breathing when I speak.	0	1	2	3	4	
6. There is often mucus in my airways.	0	1	2	3	4	
7. I have difficulties breathing during physical exertion.	0	1	2	3	4	
8. I am disturbed by leaks.	0	1	2	3	4	
9. My mask is uncomfortable.	0	1	2	3	4	
10. I receive too much air from my ventilator.	0	1	2	3	4	
11. I suffer from nasal or oral dryness.	0	1	2	3	4	
					Total	
Total divided by 11 x 2.5 →					S^3-NIV Score	

Fig. 5. S^3-NIV Questionnaire. Validated tool for assessing patient experience of noninvasive ventilation.[53]

Maximum Inspiratory and Expiratory Pressures. Measurements of maximum static inspiratory and expiratory airway pressures (P_{Imax} and P_{Emax}, respectively) isolate the strength of the respiratory muscles and thereby complement measurement of VC.[55,66] Another inspiratory pressure measure, the sniff nasal inspiratory pressure (SNIP), also assesses inspiratory muscle strength and does not require a mouth seal.[54,55,67]

Provided that these isometric respiratory efforts are indeed maximal, P_{Imax} and SNIP correlate with the strength of the diaphragm and external intercostal muscles and are strongly related to dyspnea. P_{Emax} measures primarily the strength of the internal intercostal and abdominal muscles required to generate a forceful cough. In amyotrophic lateral sclerosis (ALS), P_{Imax}, P_{Emax}, and SNIP decline earlier than sitting FVC and may thus be useful in tracking early respiratory muscle function decline in ALS.[67-70] Static pressures can be measured in a clinic using the MicroRPM respiratory pressure meter (MD Spiro, Lewiston, Maine) (Fig. 7).

Non-invasive Monitoring of Gas Exchange. As respiratory muscle weakness progresses, repeated measurement of P_{O_2} and P_{CO_2} is indicated to maintain normal respiratory gas exchange, especially during sleep. The accepted standard technique, arterial blood gas testing, should be used to confirm and accurately measure the severity of hypercapnia for hospitalized patients. However, arterial blood gas testing is generally impractical for routine monitoring of out-patients. Noninvasive assessment of S_{pO_2} is widely used as an alternative to measuring P_{aO_2} by arterial puncture.

Substitutes for direct measurement of P_{aCO_2} are also available. At a facility equipped with a nearby blood gas analyzer, venous blood can be sampled for measurement of partial venous CO_2 tension. However, because variance from simultaneously measured P_{aCO_2} is wide (bias +5 mm Hg, 95% limits of agreement 15–20 mm Hg), measurement of venous P_{CO_2} is best limited to screening for hypercapnia. In a setting of normal cardiovascular and renal function, a peripheral venous $P_{CO_2} \leq 45$ mEq/L reasonably excludes a $P_{aCO_2} > 50$ mEq/L.[71,72] An otherwise unexplained venous blood bicarbonate concentration > 27 mmol/L raises suspicion of chronic hypercapnia.[73]

Because hypercapnia reduces arterial oxygen content, pulse oximetry has long been recommended as an indirect technique for detecting hypoventilation in patients who have stable, near-normal pulmonary gas exchange. Recording oximeters can store continuously acquired data for subsequent retrieval and transmission to a nearby computer or cellular phone or by cable to a ventilator for integration into home ventilator use and function reports. Medtronic (Minneapolis, Minnesota), Masimo (Irvine, California), and Nonin (Plymouth, Minnesota) make
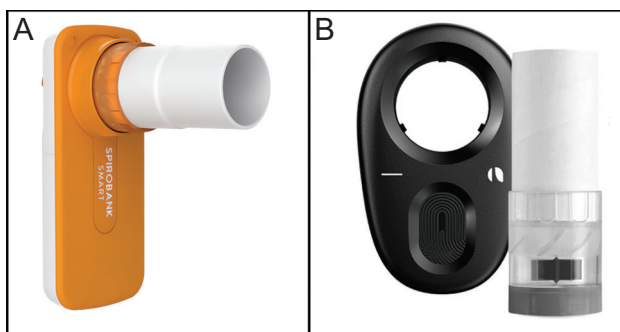
Fig. 6. Home spirometers. A: MIR Spirobank Smart spirometer; B: NuvoAir Air Next spirometer.

Fig. 7. Respiratory pressure meter. Vyaire MicroRPM respiratory pressure meter for measurement of maximum inspiratory pressure, maximum expiratory pressure, and sniff nasal inspiratory pressure.

pulse oximeters suitable for medical use. Though convenient, smart watches that offer S_{pO_2} monitoring are not sufficiently accurate to serve this purpose.

Overnight pulse oximetry becomes abnormal earlier in ALS on average than FVC.[70] However, oximetry is only about 70% sensitive in detecting mild hypercapnia in the setting of respiratory muscle weakness and is not useful for detecting hypoventilation.[74-76]

End-tidal and transcutaneous CO_2 measuring devices are available for noninvasive point-of-care estimation of P_{aCO_2}[77] although neither measurement is reimbursed for out-patient use by health care insurers in the United States. End-tidal respiratory monitors are practical and sufficiently accurate in the absence of severe parenchymal lung disease for office or home monitoring of people with tracheostomies. They are not suitable for monitoring patients during NIV.

Transcutaneous measurement of P_{CO_2} (P_{tcCO_2}) is generally considered more accurate than end-tidal P_{CO_2} measurement[78] and can be used for monitoring during mask or MPV.[48,75,79] Two companies manufacture transcutaneous blood gas monitoring devices that are currently available in the United States (Fig. 8). The Radiometer (Copenhagen, Denmark) TCM series monitors and the SenTec (Therwil, Switzerland) Digital Monitoring System are designed to approximate arterial P_{CO_2} by adjusting intradermal P_{CO_2} for temperature differences and local metabolic factors that predictably modify P_{CO_2} in the dermal microvasculature relative to arterial P_{CO_2}.[80]

For accurate results, these devices must be maintained and applied with strict adherence to the manufacturer's operating instructions. Care must be taken to apply the sensor properly to the skin at a recommended location. P_{CO_2} measured by this technique on stable out-patients has minimal bias and acceptable variance relative to simultaneously measured arterial values.[81,82] When P_{CO_2} measured by transcutaneous technique is compared to a measurement obtained simultaneously by arterial blood sampling, some of the difference is attributable to natural minute-to-minute variation in measured arterial P_{CO_2}. After correction for this effect, the 95% limit of agreement is 6 mm Hg (0.9 kPa).[83]

Transcutaneous blood gas measurements can be used in a hospital or clinic and for overnight recording in a sleep laboratory or at home.[75] When combined with home device performance data, monitoring P_{tcCO_2} can improve the efficacy of home NIV.[48,74] However, the unreimbursed operating cost can be prohibitive ($20–30 per measurement depending on the frequency of use). Some centers utilize a device from an in-patient unit or sleep laboratory for use during out-patient clinic sessions.

Cloud-Based Respiratory Device Monitoring. Most home respiratory devices internally record device use and function data for subsequent analysis. Presently, ResMed, Philips, Breas, and Ventec devices can be configured in the United States for automatic transmission of respiratory data to a central server that can be accessed online by prescribing clinicians. Other manufacturers are expected to introduce similar telemonitoring capability soon. These remote, on-demand data repositories provide out-patient clinicians with access between office visits to a wealth of information relevant to optimizing NIV including utilization data, breath rate, pressures, V_T, $\dot{V}_E$, leak, and alarm events[47,48,84] (Fig. 9). Limited evidence supports improved device performance and clinical outcomes for telemonitoring.[48,74,85,86]

Part II. Management

No universal set of rules assures effective long-term NIV. Mask selection and device application must be

Fig. 8. Home telemonitoring report. Sample detailed report from the ResMed AirView cloud-based patient management system. A 66-y-old with ALS was using an oronasal mask and an Astral ventilator set to spontaneous-timed ventilation (S/T) mode with saftey tidal volume (SV$_T$) enabled. The patient fell asleep at about 1:20 AM.

individualized. Optimal initiation of home NIV is rarely achieved in a single setup session and often requires iterative adjustment to optimize initial settings and subsequent readjustments as respiratory muscle weakness progresses or new problems arise. In addition to refinements of the settings, success invariably also requires personalized guidance and sustained coaching as patients and caregivers adapt to progressive dependence on technology. Resistance to change, gaps in understanding, and unspoken fears must be identified and addressed with compassion and patience. Skill in applying these human elements may be equally important as technical virtuosity in optimizing home ventilation for people with ALS and other neuromuscular diseases.

The physician-directed strategy described here for optimizing home ventilation is designed to achieve our proposed three goals of home ventilation through three successive phases of management: initiation, adaptation and refinement, and maintenance care. The technology for home ventilation and monitoring is advancing rapidly. Many of the recommendations detailed below have not yet been rigorously tested but instead are derived from the collective experience of clinically experienced experts in the field. Other strategies not discussed here may be equally as effective or preferable

in other settings. Recommendations are likely to change as new technologies and management insights emerge.

Indications for Initiation of Nocturnal Noninvasive Ventilation

European and United States specialists differ on indications for initiation on long-term NIV in the care of people with ALS[87] and other chronic neuromuscular diseases. In the United States, availability of ventilatory assist devices is largely determined by CMS coverage criteria[88] (Table 3). A growing, evidence-based international consensus calls for initiating home assisted ventilation earlier in the course of progressive neuromuscular respiratory disease than is supported by the current CMS criteria.[89-96] Paradoxically, the coverage criteria for respiratory assist (bi-level) devices are more restrictive and onerous than for portable ventilators or multimodality respiratory devices,[97] resulting in a large increase in inappropriate prescriptions for home ventilators in the United States, mostly for people with COPD.[98]

In 2021, the Optimal NIV Medicare Access Promotion (ONMAP) technical expert panel representing the American Thoracic Society, the American College of Chest Physicians,

Fig. 9. Transcutaneous blood gas monitor attached to the subject's left earlobe. She is wearing a nasal cushion mask.

Table 3.   United States Centers for Medicare and Medicaid Services Coverage Indications for Respiratory Assist Devices (E0471, E0471) to Treat Restrictive Thoracic Disorders

Documentation of a neuromuscular disease or severe thoracic cage abnormality, and documentation that COPD does not contribute significantly to the patient's pulmonary limitation, and one of:	
$P_{aCO_2} \geq 45$, mm Hg	Arterial blood gas sampled while the patient is awake breathing the prescribed F_{IO_2}
$S_{pO_2} \leq 88\%$ for ≥ 5 min on nocturnal pulse oximetry.	Minimum recording time 5 h while patient breathes the prescribed F_{IO_2}
For neuromuscular disease only:	P_{Imax} less negative than -60 cm H_2O or
	FVC < 50% predicted

Adapted from reference 95.
P_{Imax} = maximum inspiratory pressure

the American Association for Respiratory Care, and the American Academy of Sleep Medicine published consensus recommendations for updating CMS coverage criteria for NIVdevices.[99,100] Noteworthy among the recommendations is increasing the qualifying VC threshold to < 80% predicted if accompanied by respiratory symptoms and acceptance of an end-tidal or transcutaneous P_{CO_2} as a substitute for arterial puncture to document hypercapnia. Recommendations of the expert panel for thoracic restrictive diseases are detailed in Table 4.

For people with chronic respiratory muscle weakness, we encourage initiation of home assisted ventilation when a patient meets any of the criteria recommended by the ONMAP panel[100] or as soon as insurance coverage is available thereafter. Early initiation of therapy may be particularly important for patients with ALS because considerable lead time is often required to optimize interface selection and device settings and to fully acclimate patients to assisted ventilation. To get an early start, some patients with ALS pay to lease a ventilatory device from a durable medical equipment (DME) company while awaiting insurance coverage.

Initiation Phase

Although practice is changing,[101] many centers in Western Europe and Japan have conventionally initiated NIV during a 3–7-d hospitalization.[102,103] In the United States where few health insurance carriers cover elective admission for this purpose, hospitalization is generally limited to symptomatic individuals with a P_{CO_2} > 45–50 mm Hg who can justifiably be admitted for urgent care with a diagnosis of chronic or acute-on-chronic respiratory failure.[104] Otherwise, long-term NIV is initiated shortly before discharge from an unplanned hospitalization or in an outpatient setting.

A ventilatory support device is acquired for initiation of home care by submitting a medical order with accompanying documentation of medical necessity to a DME company. After insurance approval, a respiratory therapist employed by the company meets with the patient at home or in a retail office, fits a face mask, sets up the device as guided by the initiation prescription, and teaches the patient and/or home caregivers to operate and maintain the equipment.

Table 4. Optimal Noninvasive Medicare Access Promotion Technical Expert Panel Recommended Criteria for Initiating Bi-Level Noninvasive Ventilation for Thoracic Restrictive Disorders

Any single criterion is sufficient to initiate BPAP device for thoracic restrictive disorders.	
VC < 80% predicted with symptoms	Orthopnea, dyspnea, morning headache, daytime sleepiness, or unrefreshing sleep
VC $\leq$ 50% predicted with or without symptoms	FVC or SVC
Hypercapnia	Daytime awake $P_{aCO_2} \geq 45$ mm Hg on an arterial blood gas or
	End-tidal or transcutaneous $P_{CO_2} \geq 50$ mm Hg or
	$P_{CO_2} \geq 50$ mm Hg on a sample of peripheral venous blood gas
Oxygen desaturation during sleep*	$S_{pO_2} \leq 90\%$ for $\geq 5\%$ of the night or
	$S_{pO_2} \leq 88\%$ for ≥ 5 min
P_{Imax}	= or less negative than -60 cm H_2O
SNIP	= or less negative than -40 cm H_2O

*Can be from any pulse oximetry source, including polysomnography or home sleep test.
Adapted from reference 107.
BPAP = bi-level positive airway pressure
VC = vital capacity
FVC = forced vital capacity
SVC = slow vital capacity
P_{Imax} = maximum inspiratory pressure
SNIP = sniff nasal inspiratory pressure

Orders should specify at least the make and model of the device, the type of mask (nasal or oronasal) to be used, and the initial mode of therapy. Heated humidification is ordered to reduce the likelihood that initiation of assisted ventilation will fail because of an uncomfortably dry nose or mouth. Our orders routinely include a request for transmission of device use and performance data to a remotely assessable online data repository.

Selecting a Respiratory Device. Selection between a bi-level device, a portable ventilator, or a multimodality respiratory device for home care hinges on availability as well as technical considerations. In addition to variations in functional capabilities and limitations that bear on machine selection, bi-level devices differ importantly from portable ventilators and multimodality devices in the way United States insurance carriers pay for them.

DME providers are reimbursed for provision of RADs for patients who meet coverage criteria on a lease-to-buy arrangement.[88] CMS pays the DME company for 3 months of home use pending prescriber reevaluation after the second month and documentation of acceptable use (> 4 h per night on > 70% of nights). The DME company is then paid for up to another 10 months of use, after which time the beneficiary owns the device. DME company service support is generally limited to achieving an initial level of adherence that qualifies for extension of the rental period and then to selling replacement supplies.

Because they are considered life-support devices, portable ventilators and multimodality respiratory devices are available in the United States only through qualified DME companies. CMS includes portable ventilators in the frequent and substantial servicing payment category as they require regular servicing to avoid risk to the patient's health. DME

suppliers are paid a monthly rental fee to supply and service a home ventilator continuously until medical necessity ends. Regular home visits by a respiratory therapist and continuous on-call access to a therapist are expected.

Within the limits of insurance coverage, we start noninvasive nocturnal ventilation for patients with slowly progressive, mildly or moderately severe respiratory muscle weakness using a Bi-level capable of enabling VAPS ventilation and automatic transmission of device performance data to an online repository.

In agreement with the ONMAP Technical Expert Panel recommendations,[100] we prescribe a home ventilator instead of a bi-level device for patients with neuromuscular disease who have an FVC or SVC < 30 predicted or have previously failed bi-level support. Additionally, we prescribe a home ventilator for most people who need home assisted ventilation > 10 h a day, require peak inspiratory pressures > 25 cm H_2O or supplemental oxygen > 2 L/min after normalization of P_{CO_2}, for patients with expected rapid progression of muscle weakness, and for those with a tracheostomy in place.

Multimodality respiratory devices offer less home equipment clutter for patients who need assisted augmented airway clearance and/or supplemental oxygen in addition to ventilatory support. Highly trained caregivers are needed to interchange, maintain, and operate the several incorporated modalities. Notably, for patients supported by NIV via a single-limb passive circuit and a vented mask, each application of the cough assist modality requires manual conversion to a non-leak circuit and a non-vented face mask. Additional equipment must be attached to the device to implement the nebulizer, suction, and oxygenation functions. Because VOCSN devices do not offer a standby function, the alarm sounds continuously whenever the machine is disconnected

from the patient for setup changes or other reasons unless the alarm silence button is pressed every 60 s. Presently, we reserve VOCSN devices for selected people who leave a hospital with a tracheostomy.

Selecting a Facial Interface. Arguably, the most important decision in mask selection is whether to use a nasal or oronasal interface[105] (Fig. 10). Clinical studies published to date have reported similar efficacy for nasal and oronasal masks suggesting that selection between the two types should be individualized.[106,107] Most patients (86%) undergoing NIV included in a recent meta-analysis used an oronasal mask.[107]

People with bulbar muscle weakness may not tolerate a nasal mask because of an inability to prevent air leakage through an open mouth by closing their velopharynx. Otherwise, nasal masks are often recommended for initiation of nocturnal NIV in part because they free the mouth for cough, speech, and clearance of oral secretions or vomit. Low-profile nasal pillow and cushion masks rarely cause skin pressure injury and are preferred by many patients over nasal masks that cover the nose. However, they may be easily displaced by lateral head movement, and they tend to leak at peak inspiratory pressures > 20 cm H_2O.

Properly fitted oronasal masks often but do not always reduce open-mouth air leaks and offer a more secure interface with lateral head motion or higher inspiratory pressures. Paradoxically, oronasal masks can increase nasopharyngeal air flow resistance by applying positive pressure to the soft palate and tongue, thereby displacing those structures toward the posterior pharynx.[108,109]

For cooperative patients new to mask ventilation with normal airways, bulbar muscle function, chest wall, and lungs, we often start nocturnal NIV with a low-profile nasal cushion mask. If frequent movement of the head is anticipated, a nasal mask with a stabilizing forehead pad nasal mask may help anchor the interface in place.

Initial prescription of an oronasal mask is recommended for people who require higher peak inspiratory pressures, move frequently from side to side, or have irreversible nasal obstruction. We also recommend an oronasal mask for people who cannot breathe exclusively through their nose when they open their mouth. There are oronasal face masks that may be suitable for patients requiring inspiratory pressures > 20 cm H_2O by virtue of a large skin apposition surface that is designed to seal while minimizing pressure applied to the nasal bridge.

Selecting an Initial Device Mode. Research data published to date have not convincingly demonstrated superior outcomes for any one of the generally recommended ventilator modes over others for treatment of neuromuscular respiratory disease. However, VAPS ventilation with or without auto-EPAP enabled offers at least 2 pragmatic advantages for many patients over fixed pressure modes.[110] Subject to the limitations of the automation algorithms, initiation of assisted ventilation with automatic adjustment of inspiratory pressure can reveal variations in pressure-volume relationships during sleep that are otherwise assessable only by overnight respiratory polygraphy. Second, maintenance of ventilation in a variable pressure mode offers the potential of preserving target V_T within preset limits during respiratory infections or other acute events that reduce thoracic compliance or increase airway resistance.

VAPS should not be used as a quick "set-it and forget it" substitute for meticulous assessment and titration of device settings. The automatic options introduce a host of opportunities for setup defects that can be detected only by attentive monitoring of home device use and function data.

For PAP-naive people with stable mild or moderate respiratory muscle weakness, NIV device initiation settings are adjusted to maximize acceptance and acclimation. Reassessment and readjustment are usually required after the patient has acquired initial experience using the device at home.

Fixed Pressure Options. Many experienced clinicians preferentially start adults new to mask ventilation on home NIV using S/T mode. Properly set, this mode can ease accommodation to NIV by closely matching the patient's spontaneous breathing cycle. PC mode or S/T mode with a Timin/Timax window should be initiated instead for patients with severe respiratory muscle weakness to prevent premature cycling.

To promote patient acceptance of mask ventilation, pressures and rate are often set initially at levels below those that might be needed to normalize ventilation long term. Unless the person is known or suspected to need higher-than-minimal end-expiratory pressure to overcome upper-airway obstructive events, assisted ventilation can be introduced at an EPAP pressure of 4 cm H_2O. To initiate therapy for PAP-naïve patients, IPAP is adjusted to patient comfort, generally within a range of 8–20 cm H_2O. The backup rate can be set initially at 12 breaths/min to enable full patient control of the breath rate while preventing prolonged nonobstructive apneas during sleep. To prevent premature cycling during mandatory breaths, T_I can be set initially at 1.2 s. The advanced device settings (trigger, cycle, rise) can be deferred to the DME company respiratory therapist for titration to comfort during the initial setup. Recommended initiation settings for fixed pressure modes are shown in Figure 11.

Variable Pressure Options. We often order initiation of nocturnal NIV with VAPS enabled to gather information on overnight variability in respiratory system mechanics that is not revealed by ventilation with fixed pressures. For people with relatively normal lungs and chest cages,

Fig. 10. Face masks for home ventilation. A: Fisher & Paykel Evora nasal cushion mask; B: ResMed AirFit N20 nasal mask; C: Philips DreamWear oronasal mask; D: ResMed AirFit oronasal mask.

ventilation with AVAPS (Philips devices) or SV_T (ResMed devices) enabled is conventionally initiated at a target V_T of 8 mL/kg predicted body weight. To guide selection of a target V_T based on height, we use a unisex reference table derived from previously published predictive equations[111] (Fig. 12).

If the patient's adult standing height is unknown, height can be estimated for the purpose of selecting a target V_T by

	Philips	ResMed	
Parameter	**ST or PC**	**(S)T**	**P(A)C**
IPAP	8 - 20 cm H_2O		
EPAP	4 cm H_2O		
Breath rate	12 breaths/min		
Trigger	3 L/min or Auto-Trak	High	
Rise	3	300 ms	
Inspiratory time	1.2 s	1.0-2.0 s	
Cycle	15-25% peak inspiratory flow rate		

Fig. 11. Recommended initial settings for fixed-pressure noninvasive ventilation. S/T or (S)T = spontaneous/timed; PC = pressure control; P(A)C = pressure assist control; IPAP = inspiratory positive airway pressure; EPAP = expiratory positive airway pressure.

measuring ulna length. Equations to estimate height from that measurement have been developed using a predominantly white population by the British Association for Parenteral and Enteral Nutrition and are included in Figure 12.[112] Alternative V_T predictive equations based on ulnar length have been developed for Blacks and Asians.[113] Recommended initiation settings for variable pressure modes are detailed in Figure 13.

With VAPS enabled for patients not suspected or known to have obstructive sleep apnea, EPAP can be set initially to 4 cm H_2O. If obstructive apneas are suspected, we may instead order AVAPS-AE mode with an EPAP window of 4–12 cm H_2O and a PS window of 4–16 cm H_2O. A wide IPAP window is set initially (eg, $IPAP_{min}$ 8; $IPAP_{max}$ 20 cm H_2O) to prevent automated pressure limiting at either the low or high preset limit.

In iVAPS mode, ResMed devices can be set to calculate and apply a target alveolar ventilation based on patient height and target backup rate. Alternately, target breath rate and alveolar ventilation can be titrated by the operator to maintain a desired V_T. For iVAPS ventilation, we recommend an initial target rate of 16 breaths/min with a corresponding PS window of 4–20 cm H_2O. If obstructive sleep apnea is suspected or

Ulna Length cm		Height			PBW	Target Tidal Volume (V_T)				
Men	Women	ft, in	in	cm	PBW(kg)	5mL/kg	6mL/kg	7mL/kg	8/mL/kg	9mL/kg
		4, 4	52	132	27	135	162	189	216	243
		4, 5	53	135	29	146	176	205	234	263
		4, 6	54	137	32	158	190	221	253	284
		4, 7	55	140	34	169	203	237	271	305
		4, 8	56	142	36	181	217	253	290	326
18.5	18	4, 9	57	145	39	193	231	270	308	347
19	18.5	4, 10	58	147	41	204	245	286	327	367
19.5	19.5	4, 11	59	150	43	216	259	302	345	388
20	20	5, 0	60	152	45	227	273	318	364	409
21	21.5	5, 1	61	155	48	239	287	334	382	430
21.5	22	5, 2	62	157	50	250	300	351	401	451
22.5	22.5	5, 3	63	160	52	262	314	367	419	471
23	24.5	5, 4	64	163	55	273	328	383	438	492
23.5	25	5, 5	65	165	57	285	342	399	456	513
24.5	26	5, 6	66	168	59	297	356	415	475	534
25	27	5, 7	67	170	62	308	370	431	493	555
26	28	5, 8	68	173	64	320	384	448	512	576
26.5	28.5	5, 9	69	175	66	331	398	464	530	596
27.5	29.5	5, 10	70	178	69	343	411	480	549	617
28	30.5	5, 11	71	180	71	354	425	496	567	638
28.5	31.5	6,0	72	183	73	366	439	512	586	659
29.5	32	6.1	73	185	76	378	453	529	604	680
30		6, 2	74	188	78	389	467	545	623	700
31		6, 3	75	191	80	401	481	561	641	721

Fig. 12. Target tidal volume (V_T) look-up table. Referenced to patient height and ulna length. Reference table compiled by the authors from published data. Height to V_T conversions are derived from the prediction formulas presented in reference 117. Ulna length to height conversions derive from reference 118. This unisex table gives the same results for males as the National Institutes of Health formula for females. PBW = predicted body weight. An editable version of this table can be obtained by emailing the corresponding author.

known to be present and the optimal EPAP pressure is unknown, we initiate assisted ventilation with auto-EPAP enabled at a set window of 4–12 cm H_2O.[110]

Adaptation and Refinement Phase. Patients naïve to PAP may need to ease into home NIV starting with progressively longer adaptation sessions during the day followed by longer sessions during sleep. As they accommodate to NIV, patients with neuromuscular disease should be advised to aim for continuous use throughout sleep at night, during daytime naps, and additionally as desired for relief of uncomfortable breathing while awake.

Many patients who report comfortable mask fit and breathing during an initial device setup session do not tolerate NIV when sleeping at home. Even if treatment is tolerated, initial settings may fall short of optimizing nocturnal ventilatory support. For those reasons, NIV must be reassessed and revised as needed during a follow-up titration session scheduled within 2–3 weeks after initiation of therapy. Additional titration sessions may be needed subsequently to optimize support.

Post-Initiation Device Titration Sessions. We devote the first clinic visit after a patient has received a new or different ventilatory device to refinement of mask selection and device setup. Ideally, a physician and respiratory therapist work together during these sessions. The respiratory therapist attends to mask fit and device function while the physician focuses on patient and caregiver communication and on documentation (Fig. 14). The time required to complete and document these sessions and to coordinate the ensuing home care may qualify United States prescribing clinicians for use of the appropriate same-day prolonged care Current Procedural Terminology (CPT) billing code (G2212).[47]

If a titration session must be performed by telemedicine, straightforward adjustments to device settings can be made remotely on Philips and ResMed RADs (but not ventilators), with awareness that changes in device performance are not displayed until the next data transmission.

For more complex home titration of device settings, a DME company respiratory therapist should attend the telemedicine visit in the patient's home to adjust settings.

Noninvasive Blood Gas Monitoring. If available, a transcutaneous P_{CO_2} monitor is attached to the patient's earlobe or forehead at the outset of titration sessions to measure baseline values and to track blood gases during the session (Fig. 14). For observation periods up to 2 h in duration, probe temperature can be set safely at 44°C to maximally arterialize capillary blood under the transcutaneous sensor. P_{tcCO_2} most closely approximates arterial $P_{CO_2} \geq 10$ min after the probe is attached to the skin.[114] Operators must be aware of the 2-min delay between changes in transcutaneous and arterial blood P_{CO_2}. While the sensor warms up, we review previously

Parameter	Philips				ResMed		
	S/T AVAPS	PC AVAPS	Trilogy Legacy AVAPS-AE	Trilogy Evo AVAPS-AE	(S)T SV_T On	P(A)C SV_T On	iVAPS Auto-EPAP On
Target or SV_T	8 mL/kg Predicted Body Weight						
$IPAP_{min}$, cm H_2O	8				8		
$IPAP_{max}$, cm H_2O	24				24		
PS_{min}, cm H_2O			4				4
PSmax, cm H_2O			16				16
EPAP, cm H_2O	4				4		
$EPAP_{min}$, cm H_2O			4				4
$EPAP_{max}$, cm H_2O			12				12
Breathing frequency, breaths/min*	12						18
Trigger	3 L/min or Auto-Trak				High		
Cycle, % flow threshold	10 - 25%				10 - 25%		10-25%
Rise	3				300		
PC breath (On, Off)				On			
T_I, s	1.2						
T_I min, s				1.0	1.0		
T_I max, s				2.0	2.0		

Fig. 13. Recommended initial device settings for variable-pressure noninvasive ventilation. Asterisk indicates that on Philips devices and ResMed devices set to P(S)T or P(A)C mode, the set rate is the backup rate. On ResMed devices set to intelligent volume-assured pressure support, the default backup rate is 2/3 s the set rate. See text describing intelligent backup rate for details. S/T or (S)T = spontaneous/timed; AVAPS = average volume-assured pressure support; PC = pressure control; AE = auto-expiratory positive airway pressure; SV_T = safety tidal volume; P(A)C = pressure assist control; iVAPS = intelligent volume-assured pressure support; EPAP = expiratory positive airway pressure; PBW = predicted body weight; IPAP = inspiratory positive airway pressure; PS = pressure support; T_I = inspiratory time.

recorded home telemonitoring data and ask patients about their initial experience with home ventilation.

Optimizing Mask Fit. The patient or accompanying caregiver is then asked to don the face mask and initiate assisted ventilation using current settings. Any errors in donning technique are corrected. The face mask is checked for fit and comfort and modified or replaced if necessary.

Mask fitting can be challenging and may require several substitutions. A supply of face mask fit kits can be obtained for this purpose from sales representatives of any the major mask manufacturers. Many manufacturers include a face measurement template in their kits to facilitate correct sizing. To encourage proper fitting, the major mask manufacturers replace discarded masks purchased by DME companies at no additional charge during the first 30–60 d of use. Some patients end up using more than one face mask for different purposes or in rotation to prevent pressure-induced skin discomfort or injury.

Supplemental Oxygen. Not uncommonly, people come to initiation of home assisted ventilation after supplemental oxygen has been prescribed inappropriately for hypoxemia caused partly or entirely by unrecognized chronic hypoventilation. Whenever possible, S_{pO_2} as well as P_{CO_2} should be observed while the patient breathes ambient air on the respiratory device initiation settings. If the P_{CO_2} is < 45 mm Hg and S_{pO_2} > 94% while the patient breathes ambient air, previously observed hypoxemia at rest can be attributed to an acute decompensation or uncorrected hypoventilation, and the titration session can be continued without oxygen supplementation.

Mode and Modifications. Once a patient is wearing a comfortable face mask with an acceptable unintended leak,

Fig. 14. In-office ventilator titration session. Together with a physician, a respiratory therapist is titrating a ventilator guided in part by a P_{CO_2}, S_{pO_2}, and heart rate. The sensor is attached to the patient's right ear. The patient is wearing a nasal mask.

attention turns to refinement of device settings. If we are initiating assisted ventilation, we may start in S/T mode with target or SV_T disabled to allow direct titration of inspiratory pressure. If AVAPS is enabled during titration of a Philips device, the AVAPS rate or speed is set to the fastest available level (5 cm H_2O/min) for the duration of the session so that the machine responds quickly to changes in the set target V_T. iVAPS automatically adjusts breath by breath to changes in target alveolar ventilation.

EPAP. Contrary to a common misperception, neuromuscular respiratory disease does not protect against dynamic upper-airway obstruction.[76,115-118] At the time of diagnosis, approximately 15% of patients with ALS have moderate or severe obstructive sleep apnea.[76] If present, the default EPAP setting for NIV (4 or 5 cm H_2O) may be insufficient to reverse nocturnal apneas or hypopneas. Uncorrected upper airway obstructive events can cause patient intolerance of NIV and sleep fragmentation and associates in ALS with reduced survival.[15,76]

Assessment of people with neuromuscular disease for suspected upper airway obstructive events can be challenging. Sleep apneas cannot be observed directly during an awake titration session but must be discerned by other means. The 8-question STOP-Bang Questionnaire is widely used to screen for obstructive sleep apnea[119] but has not been validated for patients with neuromuscular disease. The utility of overnight pulse oximetry to screen people with neuromuscular disease for periodic upper-airway obstruction is limited by other influences on oxygenation during sleep in addition to upper-airway obstructive events.[76] Some individuals may be amenable to a home sleep study or an attended polysomnography

study with PAP titration at a clinical lab skilled in NIV titration. Otherwise, optimization of EPAP for home NIV requires titration in response to review of home device tele-monitoring data.

On Astral devices, EPAP adjustment can be guided by observing the machine-reported apnea-hypopnea index (AHI) during sleep in AirView telemonitoring reports (Fig. 15). Philips devices do not report AHI. If auto-EPAP was enabled on a home ventilator prior to the titration session, the EPAP pressures selected by the device during sleep can be used to guide refinement of the EPAP setting, with awareness that this automated titration is not reliable in the setting of an excessive unintended circuit leak.[110,120] If the machine-selected EPAP pressure is relatively constant overnight, auto-EPAP can then be disabled for home use. If auto-EPAP varies widely during sleep corresponding to changes in sleep stage or body position, auto-EPAP can be continued long term.

Target Tidal Volume. Target V_T should be determined and recorded for all patients undergoing home NIV. The optimum V_T balances competing objectives. Larger breaths reduce the fraction of dead space to total ventilation and minimize lung atelectasis. Smaller breaths require lower peak inspiratory pressures, thereby allowing a looser mask fit and potentially reducing unintended leak. Patient comfort should also be considered: Some may prefer larger and others smaller assisted breaths.

A target V_T of 8 mL/kg predicted body weight effectively balances those considerations for many but not all patients with chronic respiratory failure.[121] Patients with neuromuscular disease with a concomitant restrictive lung or chest
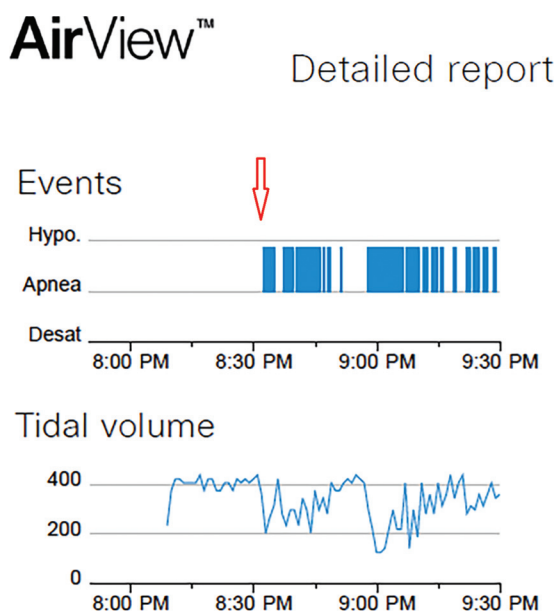
Fig. 15. Obstructive upper-airway events during nocturnal noninvasive ventilation. AirView telemonitoring report recorded by a 30-y-old with limb-girdle muscular dystrophy using an Astral ventilator set to spontaneous/timed (S/T) ventilation mode with inspiratory positive airway pressure (IPAP) 10 and expiratory positive airway pressure (EPAP) 4. The red arrow indicates the approximate time of sleep with onset of machine-identified apnea episodes and concomitant reductions in tidal volume. Titration to IPAP 16, EPAP 10 abolished the apnea events and maintained minute ventilation near the target volume of 4.2 L/min.

wall may need a target volume as low as 5 or 6 mL/kg predicted body weight to breathe with tolerable peak inspiratory pressures, as illustrated in Figure 16.

Some patients with normal lungs, including young adults long ventilated with low V_T set before completion of growth, may be initially intolerant of 8 mL/kg predicted body weight V_T. Those individuals may be best served by up titration of target V_T in small increments toward 7 or 8 mL/kg predicted body weight over weeks to several months. Conversely, some patients, notably those with cervical spinal cord injury, may be more comfortable with larger V_T (10–12 mL/kg predicted body weight or larger).[122] $V_T > 8$ mL/kg predicted body weight cause lung injury in patients with acute respiratory failure but are not known to damage the lungs of adults with chronic neuromuscular respiratory failure.

IPAP and Inspiratory Time. IPAP or PS and T_I are adjusted to maintain the target V_T during sleep and to comfortably unload patient work of breathing. Because respiratory dynamics differ considerably between awake upright breathing and breathing in different positions during sleep, adjustment of these two critical settings must be informed by home telemonitoring data in addition to direct observation during the titration session.

Start by noting whether the person or the machine is triggering most breaths. If breathing is predominantly device triggered and breaths are constant in volume in the absence of hyperventilation, IPAP and T_I can be titrated directly to the target V_T and a T_I/T_{tot} ratio between 30–45%. However, in many patients with mild to moderate respiratory muscle weakness, V_T, breath rate, and P_{CO_2} fluctuate considerably during ventilator titration sessions. This breathing pattern indicates breath-by-breath variation in patient inspiratory effort beyond that required to trigger machine-assisted breaths. Under those circumstances, IPAP cannot be titrated directly to target V_T. Attention should shift instead to comfortably unloading patient respiratory effort.

In S/T mode, starting at 4 cm H_2O > EPAP, titrate IPAP upward in 2 cm H_2O increments, observing the patient response to each change. As the applied pressure increases, cognizant patients often perceive a progressive easing of their inspiratory effort as accessory muscle use abates and breathing becomes more regular. If visibly present at the outset of titration, neck accessory muscle contraction on inspiration abates as inspiratory pressures are increased. Some patients fall promptly asleep while still sitting, suggesting severe sleep deprivation prior to the titration session. The optimal pressure setting is exceeded when the patient reports uncomfortably large breaths or peak inspiratory pressures rise sharply.

At the titrated IPAP level and prevailing breath rate, if T_I/T_{tot} is < 30% (inspiratory-expiratory ratio [I:E] < 1:2), increase T_I min or convert to PC mode and adjust T_I to patient comfort and a T_I/T_{tot} ratio 30–45% (I:E 1:2.0–1:1.2). Alternately, IPAP can be guided by enabling iVAPS on a ResMed device or AVAPS on a Philips machine.[88,123] If AVAPS or iVAPS is to be continued at home, IPAP$_{min}$ is adjusted to 2 or 3 cm H_2O below the titrated pressure. Finally, IPAP$_{max}$ is set at 6–10 mm Hg > IPAP$_{min}$ to preserve the target V_T if higher lung inflation pressures are needed subsequently because of disease progression or an acute lower respiratory infection.

Trigger and Rise. After pressures are set, check trigger, cycle, T_I, and rise to optimize patient comfort while assuring an adequate T_I. These synchronization settings are refined in response to targeted patient questions such as those shown in Table 5. Simultaneous observation of the pressure and flow curves displayed in real time on the ventilator monitor can be helpful in synchronizing device settings to patient effort.[124]

Target Minute Ventilation. Until recently, maintenance of a normal P_{CO_2} overnight during NIV could not be verified outside a sleep laboratory or an ICU. Some clinical researchers are now gaining experience recording transcutaneous P_{CO_2} during sleep at home;[79,125] however, logistical challenges and costs currently restrain widespread remote overnight use of this technology. Recording oximeters can
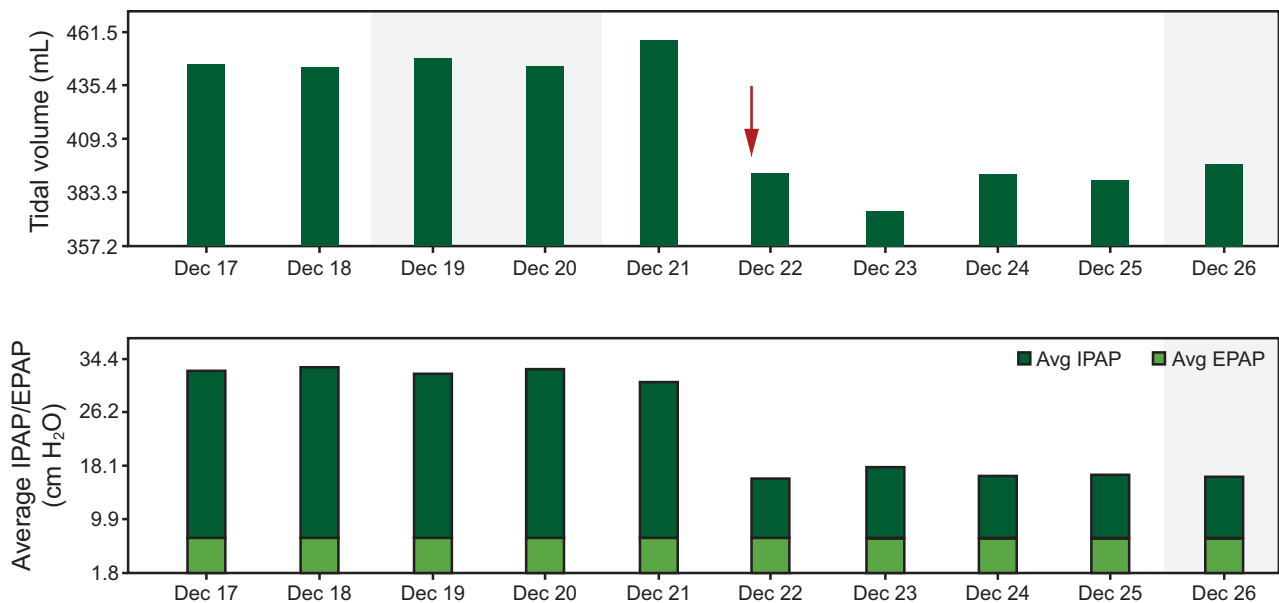
Fig. 16. Excessive inspiratory pressure. Correction of high peak inspiratory pressure by reducing target tidal volume (V_T). Care Orchestrator telemonitoring record from a 30-y-old male with severe neuromuscular scoliosis and concomitant bronchiolitis obliterans undergoing nocturnal noninvasive ventilation with a Philips Trilogy Legacy ventilator in pressure control mode with average volume-assured pressure support (AVAPS) enabled. On December 22, (black arrow) a reduction in target V_T from 440 mL (8.5 mL/kg predicted body weight [PBW]) to 350 mL (6.8 mL/kg PBW) brought about a reduction in average inspiratory positive airway pressure from 33.0 to 16.5 cm H_2O. Not shown: Total circuit leak declined from 30 L/min to 24 L/min, and breathing frequency increased from 20 breaths/min to 32 breaths/min, thereby keeping minute ventilation unchanged.

provide limited protection against uncorrected hypoventilation but do not detect machine-driven hyperventilation.

An indirect approach to maintaining P_{CO_2} within the normal range during NIV at home is available to clinicians who are equipped to measure P_{CO_2} transcutaneously or by arterial puncture during device titration sessions. The $\dot{V}_E$ that maintains a stable P_{CO_2} near 40 mm Hg during assisted ventilation in the clinic should also maintain a P_{CO_2} near 40 mm Hg during awake assisted ventilation at home provided that V_T, dead space, CO_2 production, and the rate of release of CO_2 from body stores remain substantially the same. Note that excess carbon dioxide unloads from blood and interstitium over 10–15 min after correction of chronic hypercapnia to a new quasi-steady state and more slowly thereafter from tissue stores.[126] Note also that $\dot{V}_E$ normally falls an average of 12% during sleep in healthy adults.[127] The sleep decrement has not been measured in people with neuromuscular disease but may be similar or greater.

Accordingly, the $\dot{V}_E$ observed in the clinic under steady-state conditions can be recorded as the target $\dot{V}_E$ for assisted ventilation at home. Subsequently, so long as CO_2 production and dead space remain unchanged, maintenance of the target $\dot{V}_E$ assures a reasonably normal P_{CO_2}.

If the observed P_{CO_2} during the titration session remains below the normal target during the observation period because of patient-driven hyperventilation or if a $P_{CO_2} >$ 40 is targeted, target $\dot{V}_E$ can be estimated using this equation:[128]

$$\text{Target } V_E = \frac{\text{observed } P_{CO_2}}{\text{target } P_{CO_2}} \times \text{observed } V_E$$

Breath Rate. If P_{CO_2}, V_T, and $\dot{V}_E$ are near target at this point in a titration session, the backup breath rate can be set at 2 or 3 breaths/min < the observed rate. If the patient is spontaneously hyperventilating during the session or V_T vary considerably breath to breath, the backup rate can be set using this formula:[128]

$$\text{Backup Rate} = \left(\text{target } V_E/\text{target } V_T\right) -$$
$$2 \text{ or } 3 \text{ breaths/min}$$

On ResMed devices set to iVAPS mode, the set target breath rate = 1.5 x the desired backup rate. ResMed recommends a set target rate of 15–18 for most patients. This approach encourages spontaneous assisted breathing when the patient is awake and prioritizes preservation of a near-normal P_{CO_2} over preservation of spontaneous breathing during sleep.

Final Adjustments. If AVAPS will be used at home on a Philips device, set the AVAPS rate or speed to 3 cm H_2O/min

Table 5. Questions to Assess for Patient-Ventilator Asynchrony

Question	Corresponding Settings
Does the machine comfortably trigger a breath every time you want one?	Trigger
Does the machine sometimes trigger a breath before you want one?	Trigger
After you start a breath, does the air flow in too slow, too fast, or about right?	Rise
Are your breaths too small, too big, or just right?	Cycle, PS, T_I
Does the machine end a breath too soon, too late, or at the right time?	Cycle, T_I

PS = pressure support
T_I = inspiratory time

before completion of the session. Finally, because patients and caregivers may not spontaneously complain of alarms that repeatedly interrupt sleep, check the frequency and nature of alarms recorded in the home telemonitoring report. The cause of unhelpful alarms should be determined and corrected or inactivated as appropriate. However, the circuit disconnect alarm should remain active and loudly audible for patients who cannot reliably reset a displaced face mask without assistance. Alarms should be set with special care for patients with very severe respiratory failure and for unstable, acutely hospitalized patients to guard against respiratory arrest. Ready availability of a backup ventilatory device and power supply are also appropriate for such patients.

Within 2–5 d after device titration, we review online home telemonitoring data, and the patient is asked again by telemedicine visit or telephone to report on comfort with assisted ventilation. Additional adjustments are then made as needed.

Maintenance Phase

Once nocturnal NIV is optimized, we reassess home NIV at 2–6-month intervals depending on clinical stability and anticipated rate of progression of disease. Some people may benefit from online telemonitoring check-ins between regularly scheduled visits. If properly documented, these online data monitoring assessments can be billed in the United States using the remote physiologic monitoring CPT codes 99091 or 99457,8.

With progression to severe respiratory muscle weakness, patients who initiated assisted ventilation with a bi-level device are best served by later conversion to a home ventilator. Provision of a second ventilatory device is advisable and generally covered by Medicare when a patient needs and uses a ventilator much of the day as well as at night, especially if the person uses a different setup such as MPV

while mobile in a power chair.[97] Private insurers may apply more stringent criteria for coverage of a second ventilator.

Daytime Ventilation

Daytime ventilation is indicated to alleviate daytime breathlessness and/or to correct daytime hypercapnia that persists despite optimized nocturnal NIV.[129] Because patients may not ask for daytime ventilatory support, we routinely inquire about daytime shortness of breath, fatigue, anxiety, and napping, and we measure P_{CO_2} noninvasively in the office at least twice a year.

Daytime breathing discomfort and/or hypercapnia are first addressed by verifying comfortable use of NIV throughout the duration of sleep with V_T and $\dot{V}_E$ maintained at target. For occasional periods of daytime breathlessness and for use during naps, the face mask and device settings applied at night can be extended into daytime support. For regular, more prolonged daytime use, many people are best supported by a separate, dedicated daytime NIV setup using a home ventilator that offers 2 or more presets to enable rapid, error-free transition between night and day settings.

Either or both of 2 strategies can be employed to support prolonged daytime ventilation: modified mask ventilation or MPV. With either strategy, we advise a dedicated interface fitting and device titration session to optimize day ventilation.

Daytime Mask Ventilation. People who use an oronasal mask to reduce mouth leak during sleep may prefer a nasal interface for daytime assisted ventilation to facilitate speech and oral hygiene and to reduce skin pressure injury by rotating the contact surface between day and night. Many people with intact oral pharyngeal muscle function can eat and drink while undergoing assisted ventilation with a nasal mask. However, patients with bulbar muscle weakness who cannot voluntarily close their velopharyngeal valve may not tolerate nasal NIV because of uncomfortable naso-oral air flow whenever they open their mouth.[135]

Regardless of the required nocturnal EPAP setting, many people with respiratory muscle weakness can maintain upper-airway patency while awake with EPAP set to the lowest available pressure. To facilitate speech, patients may prefer a higher IPAP pressure and a shorter rise time than used during sleep. The backup breath rate can be to 8 or 10 breaths/min to prevent undesirable machine-triggered breaths for individuals who do not ordinarily need mandatory breaths to maintain a normal P_{CO_2} when awake.

Mouthpiece Ventilation. MPV provides selected patients with on-demand ventilation for daytime use.[9,129,130] Sometimes referred to as "sip ventilation," MPV is applied via a straw-shaped or angled oral interface. The mouthpiece

Fig. 17. Mouthpiece ventilation (MPV). A: 33-y-old male with Duchenne muscular dystrophy is undergoing MPV using a single-limb passive circuit and an angled mouthpiece supported by a Philips MPV support system. B: angled mouthpiece; C: straw-type mouthpiece.

can be hand held to the mouth by the patient or supported near the patient's mouth by a semi-rigid bracket attached to a wheelchair or table (Fig. 17).

MPV differs from other modes designed for passive circuits by allowing adjustment of both EPAP and rate to 0, thereby reducing flow to an imperceptible rate between inspirations and eliminating or greatly reducing the rate of machine-generated backup breaths. Additionally, ResMed Astral and Philips Trilogy Evo ventilators offer specialized trigger settings for patients who have little or no ability to generate an inspiratory effort. The Philips *Kiss* trigger or ResMed *Touch* trigger delivers a breath cycle in response to any interruption of baseline air flow through the circuit. Patients initiate a breath by brief contact of the lip, cheek, or tongue with the tip of the mouthpiece or by pursing their lips around the mouthpiece. By means of these several features, MPV allows experienced users full control of the timing and volume of assisted breathing and full use of their mouths between breaths. People can take one breath every several minutes or continuously as desired.

MPV has limitations. Users must possess adequate cognition coupled with sufficient head, neck, and mouth control to engage, modulate, and fully disengage their lip seal at the mouthpiece. Some patients cannot prevent their cheeks from ballooning during positive-pressure inspirations. Because most alarms are disabled, MPV may be unsafe for ventilator-dependent patients who cannot summons help if the mouthpiece is displaced beyond reach. MPV may also be unsuitable for ventilator-dependent individuals prone to seizures or other unanticipated interruptions of consciousness.

Recommended Settings for Mouthpiece Ventilation. MPV can be implemented using either a single-limb passive or active circuit and either pressure or volume control ventilation.
Volume control MPV. Volume control MPV with a single-limb passive circuit is recommended by most experts for patients who can tolerate and use this mode safely. Volume control MPV facilitates breath-stacking for speech support,

cough augmentation, swallowing, and lung recruitment. To enable MPV with volume control and a passive, non-vented circuit on a Philips Trilogy Legacy ventilator, turn off Therapy and select Assist Control (AC) mode. Set the circuit type to Passive and turn on MPV. Set the flow pattern to ramp. Set the MPV Disconnect Alarm to between 1–15 min as appropriate to summon assistance if the patient unintentionally loses the ability to trigger the ventilator. Apnea and other alarms are usually deactivated for MPV.

Trilogy Evo ventilators offer a separate MPV-VC mode. This selection automatically activates the Philips Kiss trigger algorithm. Set the No Trigger alarm between 0.5–15.0 min. High and low inspiratory pressure alarms can be set or turned off. Other alarms are not available.

To employ volume controlled MPV on an Astral ventilator, install a passive, non-vented mouthpiece circuit. Select Assist Volume Control (A)CV mode. Set Trigger to Touch, PEEP to Off, and breathing frequency to 0 or a low value. On Astral ventilators, most alarms default to OFF when Mouthpiece Circuit is selected. For patient safety, the Disconnection Alarm should be set to ON with a disconnect tolerance of 60–80%. The activation time can be set between 5 s–15 min.

For volume control MPV on either Philips or ResMed ventilators, start with a large V_T, typically 800–1,500 mL, and an T_I of 1.5 s. Set PEEP or EPAP and breath rate to 0. Patients are then taught to control the inspired volume of each breath up to the limits of the preset V_T using their mouth and lips to modulate air leakage at the mouthpiece. Teach patients to breath-stack by inhaling 2 or 3 times without an intervening exhalation. Adjust V_T and T_I to comfort with attention to speaking and swallowing.

Pressure control MPV. If a patient using a Philips ventilator cannot tolerate or effectively control VC MPV, try PC MPV. To initiate PC MPV on a Trilogy Legacy ventilator, select PC mode when therapy is OFF and set MPV to ON. Set EPAP and breath rate initially to 0. Start with T_I of 1.5 s and a short rise setting. Set IPAP initially to 10 or 12 cm H_2O. Then, adjust IPAP and T_I to patient comfort in support of speech and swallowing as well as passive breathing. Set the Disconnect Alarm between 1–15 min. On a Trilogy Evo ventilator, select the MPV-PC mode. Set the No Trigger alarm between 0.5–15 min. High and low inspiratory pressure alarms can be set or turned off. Other alarms are automatically deactivated. ResMed Astral ventilators do not offer specialized settings for PC MPV using a single-limb passive circuit.

Tracheostomy

Too often, people with neuromuscular disease are discharged from the hospital after a rescue admission with an unplanned tracheostomy and inadequate preparation for long-term invasive ventilation.[131] The ensuing crisis can often be avoided by preemptive initiation and attentive maintenance of home NIV combined with early introduction of advanced care planning. With optimal care, many patients with progressive neuromuscular disease can safely maintain NIV to near total dependence on assisted ventilation.

Indications for tracheostomy include early failure of NIV caused by insurmountable upper-airway obstruction, excessive lower-respiratory secretions that cannot be cleared by antibiotics or noninvasive airway clearance, upper-airway anatomic abnormalities, or severe persistent impairment of consciousness. Tracheostomy may be preferable or required for patients moving to a skilled nursing facility or other long-term domiciliary care home. Some people with advanced respiratory failure elect tracheostomy after loss of speech and swallow to free their face and for added safety.

Individuals considering tracheostomy with the goal of extending their lives should be fully apprised of potential benefits and also the burdens of surviving on full life support with little to no skeletal muscle function. Most patients with ALS die within 2 y after acquiring a tracheostomy; however, 20% survive longer than 5 y, and some survive beyond 10 y.[132] Many report a favorable long-term quality of life including some patients who survive in a locked-in state.[132-134] However, the out-of-pocket cost to patients can reach tens of thousands of dollars a year, and the supportive care burden on family members can be crushing.[135,136] Given those considerations, < 10% of people with advanced ALS in the United States elect to undergo tracheostomy for extended survival.[137]

Regardless of indication, tracheostomy is not necessarily irreversible. After resolution of an acute deterioration that precipitated placement of a tracheostomy, selected patients can safely revert from invasive to NIV as out-patients or during a hospital stay.[138,139]

End-of-Life Respiratory Care

Increasing success in long-term application of NIV for life support has generated extraordinary challenges for the palliative and end-of-life care of patients with advanced neuromuscular disease.[140,141] As disability progresses, patients may endure multiple physical and emotional sources of distress,[142] including intense anxiety-provoking episodes of air hunger.[27] Fears of total paralysis and death by suffocation are common. Once total dependence on assisted ventilation ensues, people cannot be left alone. Family members can become overwhelmed and persistently burned out.[143-145]

Whether ventilation is assisted noninvasively or invasively, adults have a clearly established right to limit or withdraw life support that no longer serves their goals. Indeed, most United States and European patients with ALS express a preference to forego rescue hospitalizations

in favor of dying at home.[137] As an alternative to awaiting a pneumonia or other fatal event, patients with advanced neuromuscular respiratory failure who are ready to die can undergo palliative withdrawal of assisted ventilation under titrated sedation in a hospice facility or at home.[146-149] Physician-assisted suicide is legally available in several European countries and several states in the United States as an alternative for people who are not yet dependent on life support and retain the ability to ingest a fatal combination of prescribed medications themselves.[150]

Early in the evolution of advanced disease, engagement of a specialist in palliative care can elicit patient and caregiver stresses and concerns to build a well-informed platform for discussing care options near the end of life.[151-153] Conversion to hospice care should be offered at the appropriate time. We encourage active participation of respiratory medicine specialists in decisions to limit life support. For patients dependent on assisted ventilation, transition to hospice care should not preclude continued engagement of respiratory specialists in the palliative management of respiratory distress.

Part III. Troubleshooting and Problem Solving

Attainment of the 3 goals of home assisted ventilation proposed in Part I of this guide requires that patients breathe comfortably when awake and sleep soundly with normal arterial blood gases night and day. In current practice, treatment often falls short of those goals, especially for patients with ALS. Only 53% of 918 patients included in the PRO-ACT consortium registry of ALS multi-center clinical trial participants with an FVC < 50% predicted reported using NIV at the time of follow-up office visits. Fifteen percent of the 604 patients included in the registry who initiated NIV subsequently abandoned the treatment.[154] Considerably higher rates of adherence have been reported in research settings.[155-157]

Multiple risk factors for poor adherence and reduced efficacy have been identified including patient sociodemographic, neurocognitive, and behavioral attributes.[158,159] Correctable defects in mask selection or fit and device settings also contribute. A systematic approach to troubleshooting defects in device setup starts with correction of face mask discomfort, problematic air leaks, or excessive accumulation of respiratory excretions. Then, problematic upper-airway resistance and patient-ventilator asynchrony are addressed as indicated.

Face Mask Discomfort

Face mask comfort is the first prerequisite for patient adherence to therapy. Some people report a sensation of claustrophobia when first introduced to mask ventilation. Several weeks of acclimation with gradually increasing duration of use may be necessary to overcome this experience. Skin surface discomfort, discoloration, inflammation, or frank skin ulceration are common, especially when higher inspiratory pressures are applied.[40,160] First check for excessive tightening of the headgear straps. A mask that must be tightened enough to deform underlying skin does not fit well and should be repositioned or replaced with a new or different mask.

For people who experience skin injury at the nasal bridge when wearing an over-the-nose mask, try substituting an under-the-nose oronasal or a nasal cushion mask. Alternately, try nasal gel pad to protect the skin. If surface inflammation extends beyond the bridge of the nose, we advise cleaning the affected skin daily before application and cleaning the mask at least once a week with dish or hand soap. Consider replacing a mask that has a silicone cushion with one that features a gel or foam interface or a fabric mask. Alternately, try a porous cotton mask liner to redistribute pressure. The TAP PAP nasal pillow mask (Airway Management, Farmers Branch, TX) and the Bleep DreamPort mask avoid skin contact altogether except at the nares. Some patients alternate use of 2 or more masks to limit skin facial discomfort or injury.

Excessive Air Leak

Other than mask discomfort, excessive air leakage is the most common cause of intolerable or inefficacious NIV.[14,48,161-163] Problems become increasingly apparent as unintended leaks exceed 30 L/min (total leak 50–60 L/min).[164] Large leaks cause bothersome noise, facial discomfort, nasal congestion, dry mouth, sore throat, and sleep fragmentation. Large leaks dilute supplemental oxygen. Excessive unintended leak can also overwhelm device leak compensation, causing inaccurate estimates of key respiratory parameters, triggering asynchrony, and a failure to maintain target V_T.[165,166] For these reasons, correcting high leak should take precedence over addressing other ventilation parameters.

When device telemonitoring reveals excessive air leakage, check first for leaks in the tubing, connectors, or humidifier. Cracks or tears in the tubing that open between accordion folds near end connectors can be hard to find. More commonly, air leaks develop between a patient's skin or facial hair and a poorly fitted interface. Continuous mask leaks are addressed by modifying mask position or strap tension (taking care not to overtighten straps) or substituting a different interface. Intermittent leaks associated with head movement can sometimes be reduced by using a mask with an adjustable forehead stabilizer. Disruptive, non-purposeful movements common to some people with severe cerebral palsy or static encephalopathy can often be suppressed by administration of low-dose mirtazapine, risperidone, or gabapentin at bedtime.
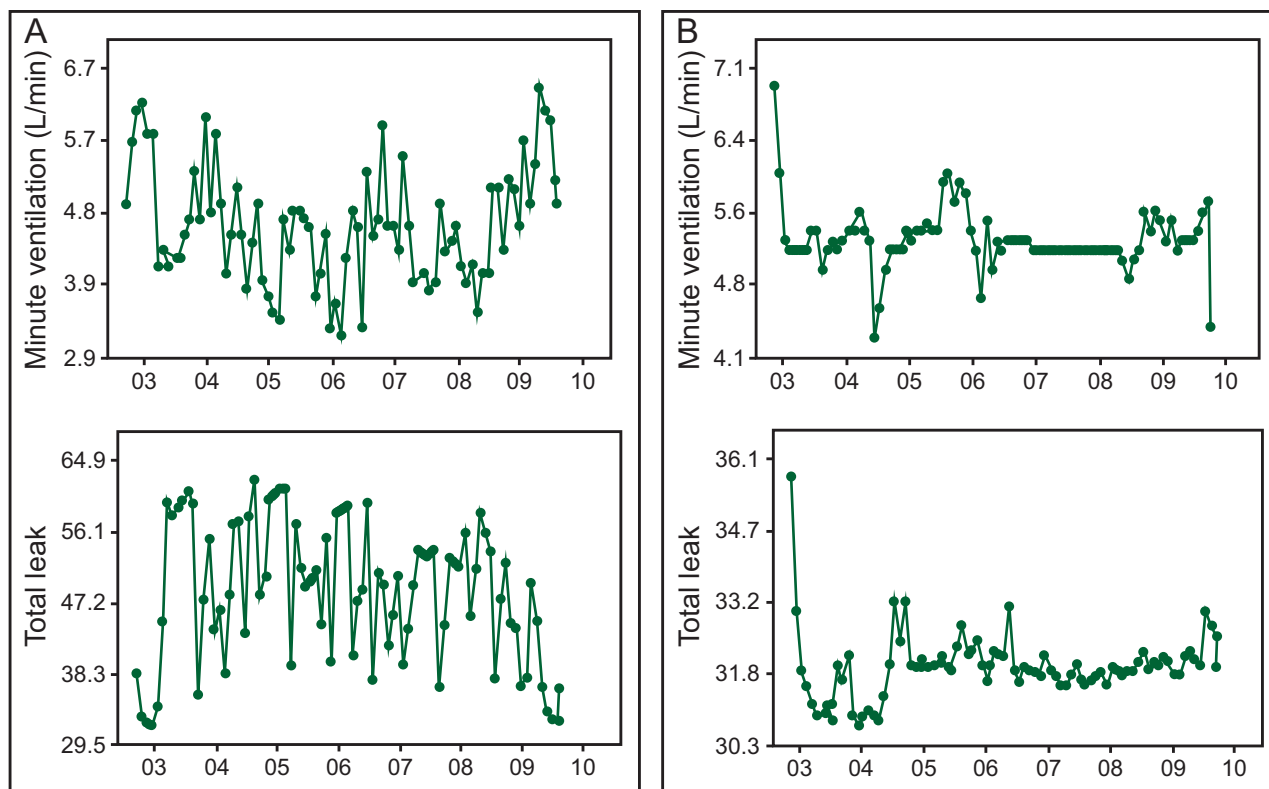
Fig. 18. Intermittent mouth leakage revealed in Care Orchestrator telemonitoring tracings recorded by a Philips Trilogy Legacy ventilator. Panel A shows a sawtooth pattern in the leak tracing suggesting recurrent mouth opening and closure. Minute ventilation ($\dot{V}_E$) is variably below the target rate (5.2 L/min). Panel B shows that addition of a chin strap greatly reduced the intermittent leak, enabling maintenance of the target $\dot{V}_E$. Note that the difference in the x axis scales between the A and B panels.

Face masks that fit well when new can acquire an excessive leak over time. The silicone, gel, or foam interface may stiffen or break down or become coated with skin oil, or the straps may stretch causing a focal leak. To avoid those problems, masks should be cleaned regularly with dish soap and water and replaced on the manufacturer-recommended schedule.

An open mouth may be the most common site of air leakage during nocturnal NIV for people with neuromuscular disease. Predisposing factors include nasal obstruction, retrognathia, weak jaw muscles, and uncorrected upper airway obstructive events. Leakage through an open mouth is suggested by an uncomfortably dry mouth despite humidification of inspired air or by lip fluttering during sleep. Intermittent, sustained episodes of excessive leak on home telemonitoring recordings suggest leakage in certain body positions. A sawtooth pattern of air leakage occurring only during sleep suggests recurrent partial awakening to close an open mouth (Fig. 18).

To prevent or reduce mouth leakage, first treat nasal obstruction and sleep apnea if present. Try avoiding a supine sleep position and excessive anterior bending of the neck. Replacement of a nasal mask with an oronasal mask may prevent excessive mouth leakage. However, air can leak through an open mouth under an oronasal mask by any of several mechanisms. Upward displacement of an over-the-nose oronasal mask may cause a leak if the lower edge of the mask rides up to appose the patient's lower lip. Use of an under-the-nose mask or full face mask effectively prevents this problem. Open mouth leaks can also occur if a relaxed jaw retracts posteriorly as the mouth opens or if application of positive pressure to the mouth induces upper-airway obstruction.[167]

A chinstrap can be applied beneath the head gear of a nasal or oronasal mask to prevent lax opening of the jaw during sleep[168] (Fig. 18). Low-profile chin straps are less obtrusive than some others but tend to shift out of position during sleep and can cause oropharyngeal air flow obstruction by pulling backward as well as upward on the jaw. Higher-profile chin straps that have worked for some of our patients are illustrated in Figure 19.

Some people with fully patent nasal and pharyngeal passages during sleep prefer mouth tape to a chin strap. Several products are available online for this purpose. A cost effective approach makes use of 3M Micropore tape (paper) or 3M Medipore tape (porous, stretchy cloth) (manufactured by 3M Science, St. Paul, MN). 1- or 2-inch wide
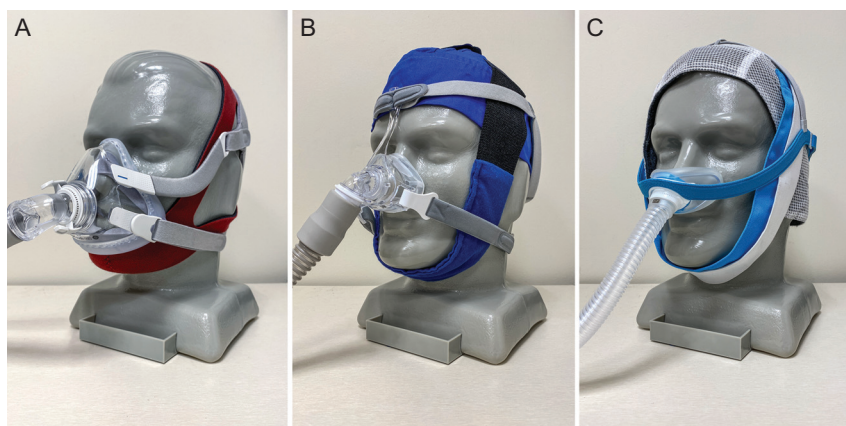
Fig. 19. Chin straps. A: CareFusion PureSom Ruby adjustable chin strap; B: Pur-Sleep PAP-Cap chin strap (Pursleep, West Jordan, UT); C: Knightsbridge Premium Dual Band Chinstrap (Knightsbridge Sleep Solutions, San Rafael, CA).
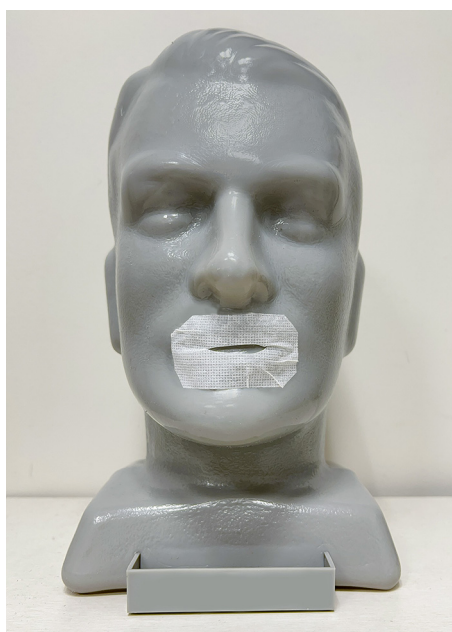

Fig. 20. Mouth tape. 3M Micropore tape cut and shaped to fit with a slit added to enable partial mouth opening.

roll tape can be torn or cut and shaped to fit horizontally or vertically. With the tape applied horizontally, a slit positioned over the lips enables speech or mouth suctioning under a nasal mask, or partial mouth breathing under a full face mask (Fig. 20). If no intervention acceptable to the patient prevents excessive mouth leak, use heated tubing to reduce mouth dryness (Fig. 3, Panel B) and increase the backup rate to compensate for smaller V_T.

Excessive Airway Secretions

People with ALS, spinal muscular atrophy, cerebral palsy, cervical cord injury, and other neuromuscular diseases that impair the oropharyngeal phase of swallowing may have trouble tolerating NIV because of an uncomfortable accumulation of pooled or partially desiccated saliva in the back of the mouth. For patients with ALS, inability to clear saliva from the mouth is a strong predictor of inability to tolerate NIV.[157,169]

Anticholinergic drugs can be used to reduce salivation with appropriate surveillance for possible anticholinergic side effects.[170] Atropine eye drops can be administered sublingually for this purpose; however, glycopyrrolate is often preferred as it is longer lasting and does not cross the blood-brain barrier. Continuous suppression of salivation can be achieved by application of a scopolamine transdermal patch behind an ear every 3 d. Additional options include benztropine or low-dose amitriptyline. Options for patients who fail pharmacologic therapy include direct targeting of salivary glands by botulinum toxin injection or radiation therapy.[171]

Accumulation of lower-airway secretions becomes problematic in the presence of lung infection, bronchitis, or recurrent aspiration. Aspiration is suggested by coughing during or shortly after eating or drinking. However, people with advanced neuromuscular disease may not cough when they aspirate. The oropharyngeal phase of swallowing can be assessed safely in the clinic with the assistance of a speech pathologist and a mobile laryngoscopy cart by fiber-optic endoscopic evaluation of swallowing.

In the presence of reduced cough strength, chest congestion indicates a need for manual or mechanical cough augmentation.[172] Patients with persistent problematic aspiration caused by oropharyngeal dysfunction may need to undergo placement of a gastric feeding tube and forgo oral feeding. Some are best served by a tracheostomy to enable airway clearance using a suction catheter.

Upper-Airway Resistance

Fixed or dynamic obstruction of the nasal passages or pharyngolarynx commonly impairs NIV. Detection and rectification can be challenging.

Increased nasal resistance to air flow may be anatomical or inflammatory in origin or precipitated reflexively by positive-pressure ventilation. Nasal obstruction predisposes to recurrent upper-airway collapse and can reduce tolerance of PAP therapy.[173] Allergic rhinitis and bacterial or fungal sinusitis should be treated pharmacologically with an antibiotic, nasal saline rinses, or an intranasal corticosteroid as appropriate. Non-allergic nasal obstruction that develops during the night may respond to an inhaled nasal antimuscarinic agent or by using heated tubing to maximize the transfer of inhaled moisture to the nasal passages (Fig. 3, Panel B). A nasal mask can be replaced by an oronasal interface to bypass persistent nasal passage obstruction. Some individuals with prolonged life expectancy may opt for surgical intervention to correct obstructing anatomic defects. Patients with limited life expectancy may benefit from nightly use of long-acting inhaled oxymetazoline or another topical sympathomimetic decongestant, with awareness that regular use of these drugs can cause troublesome rebound nasal congestion if discontinued (rhinitis medicamentosa).

In neuromuscular disease, uncorrected dynamic pharyngolaryngeal obstruction may be the second most important device-associated cause of uncomfortable or ineffective NIV after excessive air leak.[8,15,109,174,175] Most of these obstructive events respond to replacing an oronasal mask with a nasal mask or by increasing EPAP as high as 12 or 14 cm H_2O.[108,109] However, recent studies have identified clinically consequential upper-airway events that are not responsive to either intervention in some patients with bulbar ALS.[109]

One such pattern, termed upper-airway obstruction with decreased central drive (ODCD), is characterized by active expiratory glottic closure with concomitant central apnea.[15,175] These events appear to result from a combination of upper motor neuron hyperirritability and instability in the central control of breathing. Machine-driven hyperventilation predisposes to these events.[15] ODCD causes ineffective ventilation during sleep and is associated with reduced survival.[15] Several treatment strategies have been suggested, but none has been rigorously tested to date.[175]

Other patients with ALS and dysphagia complain of an intolerable choking sensation that may result from accumulation of inspissated saliva driven to the back of the mouth by oral application of PAP. Conversion from an oronasal to a nasal mask and titration of anticholinergic agents may help. Patients with bulbar ALS who cannot tolerably achieve effective ventilation may consider early conversion to a tracheostomy.

Patient-Ventilator Asynchrony

Patient-ventilator asynchrony refers to a mismatch in breath rate, inspiratory flow, or duration of inspiration between the neural effort of the patient and a positive-pressure cycle applied by the ventilatory support device.[48,174,176,177] These defects in NIV are common, especially during sleep.[166] Mild or occasional patient-ventilator asynchronies are generally tolerated. Frequent or severe asynchronies can cause uncomfortable breathing, anxiety, upper-airway obstructive events, below target V_T, or poor sleep quality and may reduce survival.[15,166]

Three types of ventilator asynchrony are described. Rate asynchrony occurs when the machine fails to respond to patient initiation of a breath (ineffective triggering) or spontaneously triggers unwanted breaths (double triggering or auto-triggering). Excessive circuit leak and dynamic upper-airway obstruction are common causes of rate asynchrony.

Cycle asynchrony occurs when the device detrimentally reverts from IPAP to EPAP pressure before (premature cycling) or after (delayed cycling) the end of a person's inspiratory effort ends. The third type, inspiratory flow asynchrony, develops when the inspiratory flow generated by the machine undershoots or overshoots the patient's desired inspiratory flow.[166]

Clinically important asynchronies can often be detected during a device titration session by visual observation of patient respiratory effort combined with focused questioning (Table 5). In addition, breath-by-breath pressure and flow waveforms can be observed in real time on ResMed and Philips ventilator monitoring panels. Trilogy Evo ventilators store high-fidelity waveforms (pressure, flow, volume, and total leak) for 31 d. These data can be downloaded from the ventilator to a USB flash drive and then uploaded through a computer to Care Orchestrator for subsequent analysis (Fig. 21). Similar recorded data are assessable on ResMed Astral ventilators using ResScan software.[48] Reliable classification may require a full polygraphic sleep study.[174] Once characterized, asynchronies that persist after correction of leak and upper-airway obstruction generally respond to adjustments in the settings for trigger, cycle, and T_I.[174,178]

Aerophagia

Many people undergoing positive-pressure ventilation report an increase in eructation and flatulence, especially early after initiation of PAP therapy. Some are troubled by persistent uncomfortable abdominal bloating. Severe abdominal distention can compromise breathing by exerting cephalad pressure on the diaphragm.

A reduction in peak inspiratory pressure may reduce passage of air into the stomach. Replacement of a full face with a nasal mask may help. Persistent problematic abdominal bloating unresponsive to changes in respiratory device settings implies a concomitant defect in gut motility or small bowel intestinal overgrowth warranting consultation with a gastroenterologist. Refractory gastric air distension
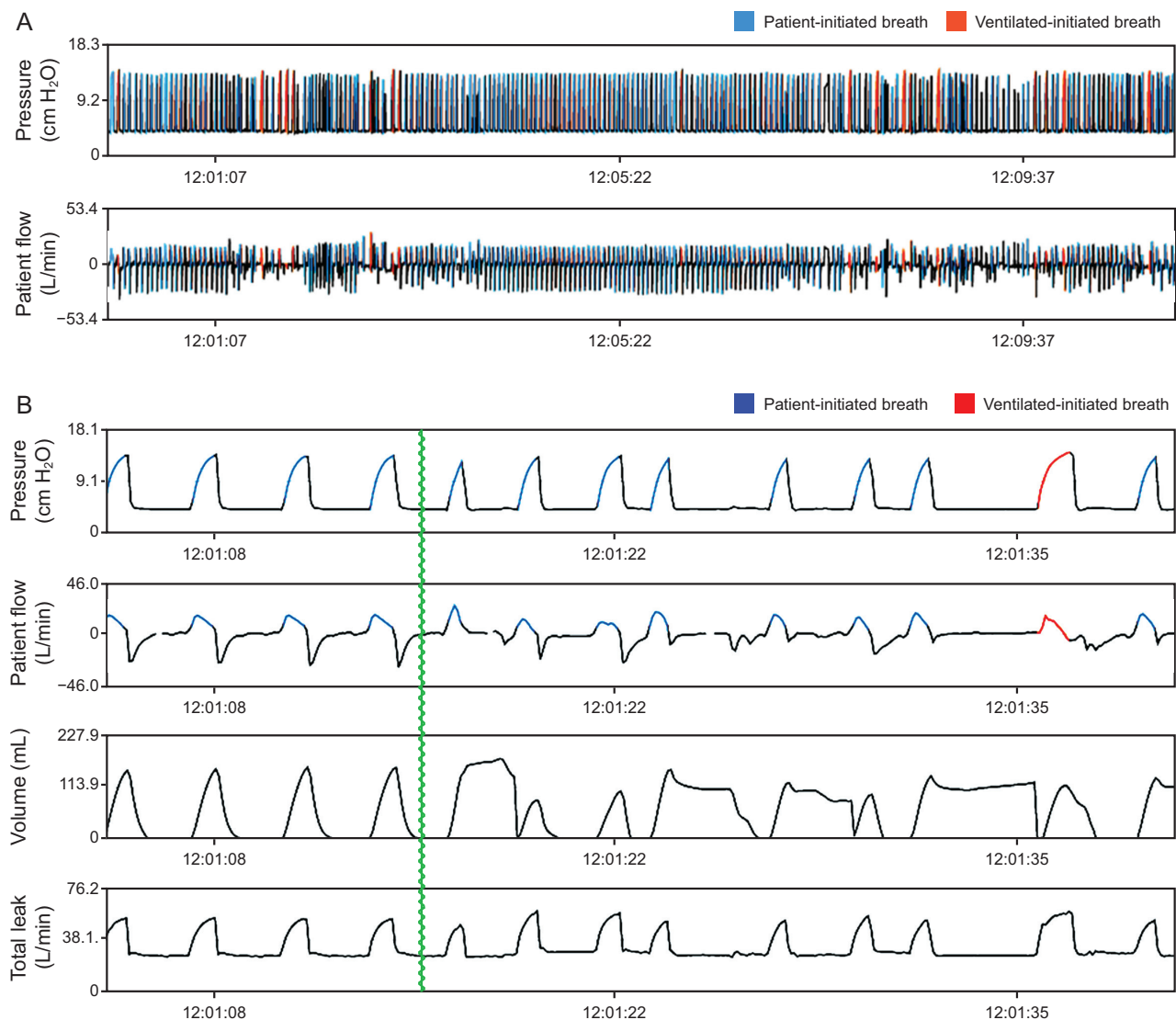
Fig. 21. Nocturnal waveform recording. Download of waveforms recorded at home by a Philips Trilogy Evo ventilator. Panel A shows an epoch of approximately 8-min duration recorded during sleep with intermittent irregularities in the pressure and flow curves. Panel B shows an epoch of approximately of approximately 30 s duration. The vertical green line marks the onset of an episode of asynchronous breathing. Note variable breath intervals and tidal volumes suggestive of awakening with variable patient inspiratory effort.

can be relieved by venting air from the stomach through a nasogastric or percutaneous gastric tube. As needed, opening of a stopcock attached to the external tip of the gastric tube between feedings may suffice. Use of a Farrell valve bag allows continuous decompression of the stomach into a closed, sterile system. Placement of a gastro-jejunal tube enables intermittent or continuous venting of the stomach during tube feeding.

Conclusion

Chronic physiological derangements as diverse as hypertension, diabetes, end-stage renal disease, and glaucoma are managed quantitatively. Treatment is initiated and modified as needed to maintain measurable indices of bodily functions within normal ranges. Only recently have monitoring tools become widely available to enable quantitative optimization of home assisted ventilation. The data-driven treatment strategy offered in this guide demonstrates the potential of current technology to achieve all 3 of our proposed goals for long-term ventilatory support.

The recent technological advances have also revealed gaping shortcomings in current evidence-based knowledge on how best to manage chronic respiratory failure. Too often, the justification for recommendations we have passed

along from previous authors and those we have proposed anew are justified by little more than "this is what we do." Consensus is lacking on what constitutes "optimal" home assisted ventilation and what applications of technology best achieve optimal support. Information is particularly needed regarding the cost-effectiveness of transcutaneous P_{CO_2} measuring devices to guide normalization of home ventilation. Attention must also be directed to the ethical challenges that arise when the lives of people with profound physical disability can be prolonged for years or decades.

These many opportunities and challenges have given rise to a new medical specialty focused on chronic respiratory failure. Formal training pathways are needed to prepare clinicians for this promising specialty at the interface between pulmonary, critical care, and sleep medicine.

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