Measuring Adherence to Long-Term Noninvasive Ventilation

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BACKGROUND: Obtaining benefits from long-term noninvasive ventilation (NIV) relies on achieving adequate adherence to treatment. Reported adherence to NIV is variable and could be influenced by high-volume users and attrition of nonusers and those who die. This observational study aimed to describe patterns of use and adherence rates in new unselected users of NIV. METHODS: All adults (> 18 y old) commencing long-term NIV were consecutively enrolled and followed for 6 months. Ventilator data were manually downloaded from devices and usage (minutes per day) was collected. Subjects were categorized into adherent users ($\geq$ 4 h/d) and nonadherent users (< 4 h/d). RESULTS: Data were obtained from 86 subjects. Most (65%) had motor neuron disease, and most commenced NIV in an out-patient setting (72%). At one month after NIV implementation, overall average daily use was 302.1 min/d and categorical adherence was 57%. At 6 months or prior to death, overall average daily use increased (388.7 min/d), but categorical adherence was similar (62%). The majority of subjects (84%) remained in the same adherence category from their first month to their sixth month of use or death. Individuals with motor neuron disease demonstrated significantly lower rates of adherence compared to the rest of the cohort at 1 month (48% vs 73%, $P = .03$). In those who died within the study period ($n = 19$, all with motor neuron disease), this difference persisted to death (42% at death vs 73% at 6 months, $P = .032$). CONCLUSIONS: Average daily usage may conceal true prevalence of adherence or nonadherence to NIV within a population. Reporting both average daily use data and categorical adherence rates (using a threshold of 4 h/d) may improve transparency of reported outcomes from clinical trials and identifies a therapeutic target for home mechanical ventilation services for quality improvement. *Key words: noninvasive ventilation; patient compliance; respiratory insufficiency; treatment adherence.* [Respir Care 2021;66(9):1469–1476. © 2021 Daedalus Enterprises]

Introduction

Noninvasive ventilation (NIV) is an effective treatment for chronic hypercapnic respiratory failure related to neuromuscular disorders including motor neuron disease (MND), as well as other disorders like COPD, obesity hypoventilation syndrome (OHS), and restrictive thoracic disorders.[1-3]

The benefits of NIV for survival, symptoms, and health-related quality of life are, however, reliant on adequate adherence to treatment.[4-7] Lack of consistent use of NIV is likely to degrade its benefits. Hence, monitoring and intervening to improve adherence to therapy are important

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strategies for clinical trials and home mechanical ventilation (HMV) services.

A threshold of at least 4 h of NIV use per day appears to be important to improve arterial blood gas parameters, symptoms, and respiratory function.[5,8-10] In addition to the adequacy or quality of ventilation, such as patient-ventilator synchrony and normalization of arterial blood gases, this adherence threshold of 4 h of NIV is considered an important prognostic factor, particularly in patients with MND.[5,11-13] For other diagnoses, lower levels of adherence may still confer a clinical benefit, but this has not been demonstrated conclusively. Many studies evaluating long-term NIV have reported average daily usage (ie, in minutes or hours per day) in a population, rather than categorizing proportions of good and poor adherers to treatment.[3,14-18] If NIV use within a population increases over time, such as in progressive neuromuscular disorders, this may give the impression of overall improvements in adherence, whereas an increase may actually reflect worsening respiratory failure.[19] Additionally, high-volume users of NIV and attrition of low-volume or nonusers may mask true adherence data within a population.

Reports of adherence to long-term NIV are therefore varied, ranging from 40–50%[20,21] to 60–70%.[22-24] Adherence data have often been incomplete or have not been reported categorically or consistently.[2,3,18,25,26] Outside of controlled clinical trials, the reported data are also variable in observational and cross-sectional studies, with reported adherence rates ranging from 40–55%[10,21,27-29] to 75–95%.[6,22,30-36] The aim of this observational study was to describe patterns of use and adherence rates in unselected, new users of long-term NIV from a single, centralized HMV service.

Methods

This observational study was performed by the Victorian Respiratory Support Service, a statewide specialist HMV service based in Melbourne, Australia. Approval was obtained from the Human Research Ethics Committee at Austin Health (Melbourne, Australia) as a quality improvement initiative. All adults (> 18 y old) commencing NIV were consecutively enrolled and followed for 6 months. Those who were commenced on invasive ventilation or CPAP were excluded from the analysis. A convenience sample of 100 subjects was chosen, and data were evaluated at 6 months after commencement or after death in those who died within 6 months.

Detailed descriptions of the structure and routine care provided within this HMV service have been described previously.[37] The service manages domiciliary ventilation across the state of Victoria, Australia and is located within a large tertiary health service. The HMV service incorporates an in-patient medical team, trained respiratory physiotherapists, and other allied health staff. Community outreach is

QUICK LOOK

Current knowledge

Obtaining benefits from long-term noninvasive ventilation (NIV) relies on adequate usage, otherwise known as adherence to treatment. At least 4 h of NIV use per day appears to be important for improvements in physiological parameters, quality of life, and survival, particularly in patients with conditions such as motor neuron disease. Many clinical trials report average daily use of NIV (in minutes or hours per day) as a measure of adherence to treatment.

What this paper contributes to our knowledge

This observational study of a comprehensive cohort of unselected, new users of long-term NIV indicates that average daily use does not reflect true adherence and nonadherence to treatment in a population. While all groups achieved average usage > 4 h/d, this did not correspond to adherence rates when individuals were categorized using a threshold of 4 h/d. Average daily use is a potentially misleading quality metric in a population compared to categorical adherence rates.

facilitated by specialist nurses and includes a 24-h telephone support line and regular multidisciplinary out-patient clinics (both in-person and via telehealth consultations). Prospective clients are referred to the HMV service from other health services or from the community. Clients who are referred during an acute in-patient stay at another health service are typically transferred from the referring center to enable NIV implementation. Individuals who are suitable for elective commencement of HMV do so either during a scheduled in-patient admission or using a "day admission" ambulatory out-patient care model.[38] The outreach service provides home visits to clients who are unable to attend clinic, although these are not routine and home implementation of NIV is not undertaken. In-lab polysomnographic titration of NIV is the standard of care, with this approach utilized to titrate and evaluate the effectiveness of ventilation.[24] Airway clearance techniques are prescribed on a case-by-case basis. All clients are encouraged to consider advanced care planning.

This observational study was performed with usual clinical procedures for the service, with all subjects administered NIV by specialist respiratory physiotherapists during either a multi-day in-patient admission or, more commonly, during a day admission.[38] The decision to commence NIV was made at the discretion of the referring HMV physician, with indications consistent with local and international recommendations.[39-41] Prior to discharge, all subjects and their caregivers were provided with a standardized education session regarding use and maintenance of the NIV

Table 1.   Subject Characteristics

Male	54 (63)
Female	32 (37)
Age, y	61 (18–89)
Diagnosis	
Rapidly progressive disease	
Motor neuron disease	56 (65)
Stable or slowly progressive diseases	30 (35)
Other neuromuscular disease	15 (17)
Obesity hypoventilation syndrome	6 (7)
Restrictive thoracic disease	5 (6)
COPD	4 (5)
Residence	
Metropolitan	60 (70)
Regional	26 (30)
Location of care	
Out-patient (day admission)	62 (72)
In-patient admission	24 (28)
PSG-assisted titration	55 (64)

Data are presented as *n* (%) or mean (range). *N* = 86 subjects.
PSG = polysomnography

equipment. An instruction booklet and contact telephone numbers were provided, and subjects were encouraged to contact the outreach nursing service if they experienced any issues with using NIV at home. After NIV implementation, subjects were routinely referred to return for overnight polysomnography to optimize NIV parameters.[24]

At 6 months after NIV implementation, ventilator data were obtained during routine clinical interactions or via mail, with manual data downloads using data cards or USB drives depending on the device. All data were obtained from ResMed ventilators (VPAP IV, Stellar 150, and Lumis; ResMed, New South Wales, Australia), which were allocated to subjects based on clinical need. Remote data monitoring was not undertaken. NIV usage in minutes per day (min/d) was collected; subjects were categorized by usage per day (ie, 0–1 h, 1–4 h, and ≥ 4 h per day), and chi-square analysis performed. Additional demographic and clinical data (including date of death) were obtained from the HMV service database. Detailed clinical information such as specific therapeutic interventions, complications, hospitalization, and cause of death were not collected.

Results

From June 1, 2017, to January 12, 2018, 100 individuals were commenced on NIV through the HMV service and followed for 6 months. Data were obtained from 86 of the 100 NIV users. Data were missing due to malfunctioning ventilator data storage (*n* = 3) and failure to attend for follow-up (*n* = 11). The majority of this population (*n* = 10), had either MND or another neuromuscular disorder (NMD). Reasons

for recurrent nonattendance were not provided for 8 subjects; 1 subject refused to attend, citing excessive burden, while the remaining 2 subjects had relocated residence or were not contactable despite repeated attempts. These 14 cases were excluded from the analysis.

Fifty-six of the remaining sample of 86 subjects had an underlying diagnosis of MND (Table 1). Average age was 61 y; most subjects were male (63%) and resided within metropolitan Melbourne (70%). The majority (72%) were implemented electively on NIV as a day admission. The majority (64%) underwent subsequent polysomnography to optimize NIV settings.[24] According to the HMV database entries, subjects interacted with staff from the HMV service a median of 5 times during the study observation period (range 0–22 interactions). Mortality at 6 months was 22% (*n* = 19); all of the deceased subjects had a diagnosis of MND. Ventilator settings at implementation and at 6 months or the month of death are described in Table 2.

For the whole cohort (*N* = 86), overall average usage at 1 month and at 6 months or the month of death was 302.1 min/d and 389.4 min/d, respectively. In survivors at 6 months (*n* = 67), overall average usage was 388.7 min/d (Fig. 1). When analyzed according to diagnostic groups, all groups appeared to have satisfactory daily usage of ≥ 240 min (≥ 4 h) across the 6 months following NIV implementation (Fig. 1). Those with MND had similar average daily use at 1 month, when compared to the rest of the cohort (267.3 min/d vs 302.1 min/d, *P* = .44).

However, when individuals were categorized using a 4-h threshold, adherence was significantly lower in the MND group at 1 month than the remainder of the cohort (27 of 56 [48%] vs 22 of 30 [73%], *P* = .03) (Table 3). In those with MND who died within the study period, this difference persisted to death (8 of 19 [42%] vs 22 of 30 [73%], *P* = .032). Among survivors with MND at 6 months (*n* = 67), the categorical adherence rate was 62% (23 of 37), which was similar to those with other diagnoses at 6 months (23 of 37 [62%] vs 22 of 30 [73%], *P* = .34) (Table 3).

Although average daily use increased for the overall group and in most diagnostic groups except those with OHS and stable NMD (Fig. 1), categorical adherence was relatively stable over the 6 months (Fig. 2). Overall, at 1 month, 57% of subjects were adherent, increasing marginally to 62% at 6 months or the month prior to death (Table 3). While there appeared to be a larger increase in adherence in the MND group from 1 month (48%) to 6 months (62%), this reflected the behavior of survivors once the 19 subjects who died within the study period were accounted for (Fig. 2). The majority of subjects (84%) remained in the same category of adherence from their first month of use to their sixth month of use or the month prior to death (stable adherence: *n* = 43 [50%]; stable nonadherence: *n* = 29 [34%]). Overall, 9 subjects shifted from nonadherent to adherent, and 5 subjects changed from adherent to

Table 2. Ventilator Settings

	Overall (N = 86)		MND (n = 56)		Other NMD (n = 15)		OHS (n = 6)		RTD (n = 5)		COPD (n = 4)	
	Implement	6 Months or Prior to Death	Implement	6 Months or Prior to Death	Implement	6 Months	Implement	6 Months	Implement	6 Months	Implement	6 Months
IPAP, cm H_2O	13.4 ± 4.1	14.2 ± 4.5	11.9 ± 2.7	12.7 ± 3.1	14.1 ± 2.8	14.7 ± 4.8	21.0 ± 3.9	21.7 ± 3.9	16.8 ± 6.4	19.6 ± 4.3	15.8 ± 5.6	15.8 ± 5.6
EPAP, cm H_2O	6.7 ± 3.3	7.3 ± 3.6	5.6 ± 2.2	6.1 ± 2.6	6.8 ± 2.5	8.0 ± 3.9	12.8 ± 3.1	13.2 ± 3.1	9.0 ± 5.2	9.8 ± 4.3	9.3 ± 3.4	9.3 ± 3.4
BURR, breaths/min	13 ± 2	14 ± 2	13 ± 2	13 ± 2	14 ± 2	15 ± 2	12 ± 2	12 ± 2	14 ± 2	15 ± 3	13 ± 2	16 ± 2
T_I minimum, s	1.0 ± 0.1	1.0 ± 0.1	1.0 ± 0.1	1.0 ± 0.1	1.0 ± 0.1	1.0 ± 0.1	1.0 ± 0.1	1.0 ± 0.1	1.0 ± 0.1	1.0 ± 0.1	0.9 ± 0.1	1.0 ± 0.1
T_I maximum, s	1.6 ± 0.1	1.6 ± 0.1	1.6 ± 0.1	1.6 ± 0.1	1.5 ± 0.1	1.5 ± 0.1	1.6 ± 0.1	1.6 ± 0.1	1.5 ± 0.1	1.5 ± 0.1	1.5 ± 0.1	1.4 ± 0.2

Data are presented as mean ± SD.
MND = motor neuron disease
NMD = other neuromuscular disease
OHS = obesity hypoventilation syndrome
RTD = restrictive thoracic disorders
IPAP = inspiratory positive airway pressure
EPAP = expiratory positive airway pressure
BURR = backup respiratory rate
T_I = inspiratory time

nonadherent. A comprehensive assessment of potential factors that may have influenced adherence within this cohort was not performed, although location of implementation, use of polysomnographic titration, and residential location demonstrated trends in adherence rates that may warrant further exploration in controlled trials (Table 4).

Discussion

Consecutive individuals commencing NIV at a single Australian HMV service demonstrated overall adherence similar to that described in other reports.[20-23] At 1 month, overall average daily use was 302.1 min/d and categorical adherence was 57%. At 6 months or the month prior to death, overall average daily use increased (388.7 min/d) but categorical adherence was similar (62%). Individuals with MND were the largest group within this cohort of new users but also demonstrated the highest rate of nonadherence with NIV. Although adherence among those with MND appeared to improve over time, these results confirm that this apparent trend was primarily due to a higher mortality rate among users who were nonadherent with NIV.

An important finding from this study is evidence of the potentially misleading difference between average daily use and categorical adherence rates. While all diagnostic groups and the overall cohort demonstrated an apparently satisfactory level of average daily use (≥ 4 h/d) (Fig. 1), this did not correspond to adherence rates when presented categorically (Table 3). Prior to this study, it was suspected that that nonadherence was common but essentially hidden from clinicians due to attrition bias (eg, death and loss to follow-up), and these results have in many ways confirmed this suspicion. We speculate that similar findings would be observed in unselected cohorts of new users of long-term NIV from other locations. This nonadherent cohort, therefore, should represent a tantalizing therapeutic challenge for clinicians and researchers to address.

In one of the largest studies of long-term outcomes and mortality in different patient groups on HMV, Schwarz and colleagues[6] reported that daily NIV usage was associated with time to death even when correcting for age, gender, and diagnosis. Despite significant differences in mean daily use across different disease groups, there was a significantly longer time to death in subjects who used NIV for > 4 h/d compared to those who used NIV for shorter periods. Similarly, a large study by Patout et al,[7] who investigated long-term outcomes from 2 European HMV services, indicated that adherence to NIV of > 4 h per night was associated with improved survival. More recently, Ackrivo et al[13] reported on a large retrospective study in individuals with MND, in which NIV use was associated with a reduction in the rate of death and there again appeared to be improved survival in those able to achieve average use
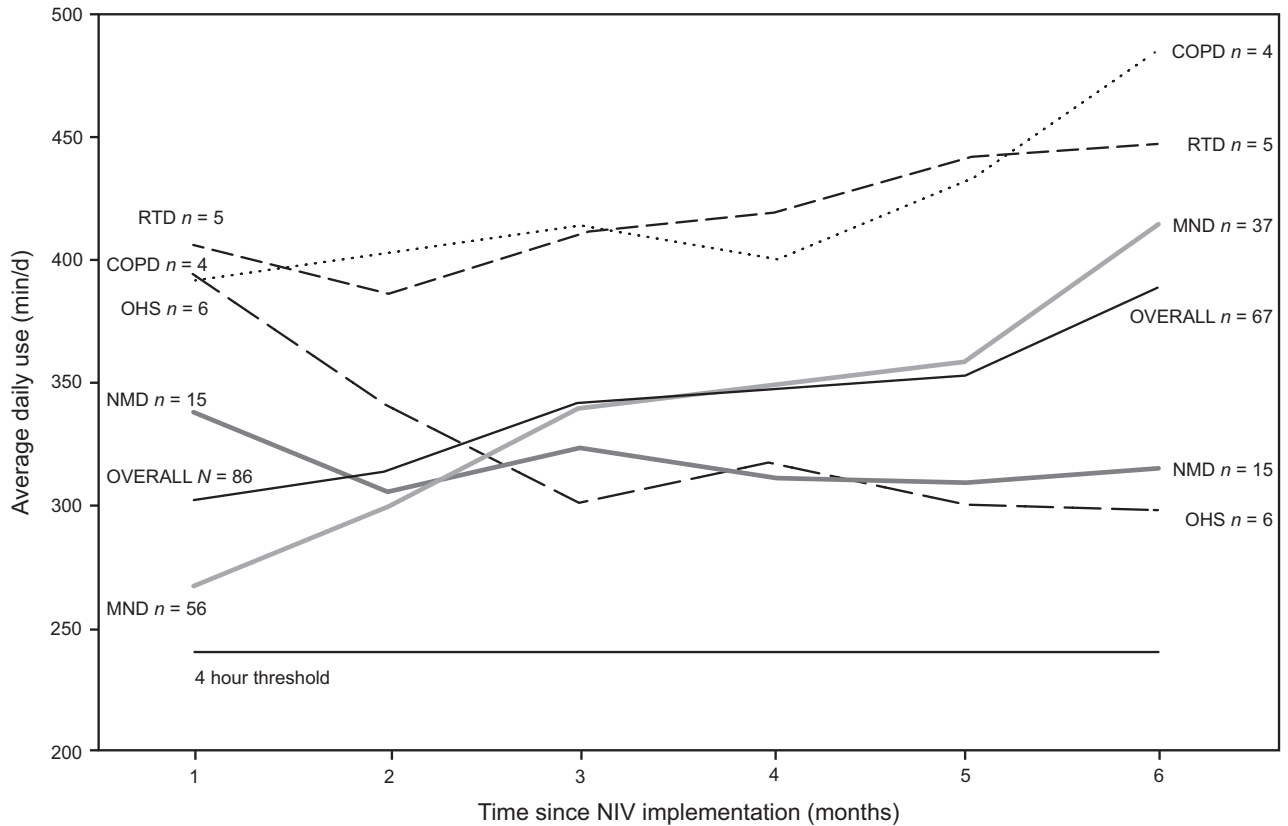
Fig. 1. Average overall daily usage. Raw average minutes/day of noninvasive ventilation (NIV) over the first 6 months of use (in subjects alive per month). All deaths were in the MND group ($n = 19$). MND = motor neuron disease; NMD = other neuromuscular disease; OHS = obesity hypoventilation syndrome; RTD = restrictive thoracic disorders.

Table 3. Categorical Adherence Thresholds for NIV Usage

Average Daily NIV Usage	Overall (N = 86)		MND Overall (n = 56)		MND Died ≤ 6 Months (n = 19)		MND Survivors at 6 Months (n = 37)		Stable or Slowly Progressive Disease* (n = 30)	
	1 Month	6 Months or Prior to Death	1 Month	6 Months or Prior to Death	1 Month	Prior to Death	1 Month	6 Months	1 Month	6 Months
0–1 h	23 (27)	20 (23)	20 (36)	15 (27)	6 (32)	8 (42)	14 (38)	7 (19)	3 (10)	5 (17)
1–4 h	14 (16)	13 (15)	9 (16)	10 (18)	4 (21)	3 (16)	5 (13)	7 (19)	5 (17)	3 (10)
> 4 h[†]	49 (57)	53 (62)	27 (48)	31 (55)	9 (47)	8 (42)	18 (49)	23 (62)	22 (73)	22 (73)

Data are presented as n (%).

* Includes individuals with neuromuscular disease other than MND, restrictive thoracic disorders, obesity hypoventilation syndrome, and COPD.

[†] > 4 h = adherent users

NIV = noninvasive ventilation

MND = motor neuron disease

of > 4 h/d when compared to those with an average use of < 4 h/d.[42] Until further studies can demonstrate that lower (or higher) thresholds should be used, a 4-h threshold appears appropriate and clinically relevant. Future studies describing NIV adherence should consistently report both average daily use and categorical adherence rates. Such a reporting schema should assist in avoiding group mean behavior obscuring this important population outcome data.

Another finding from this study is that adherence patterns may be established soon after commencing long-term NIV, with most users establishing a pattern of use within the first month of therapy. Vandenberghe et al,[35] investigating factors that predicted tolerance of NIV in patients with amyotrophic lateral sclerosis, also reported that early tolerance to NIV predicted future usage at 1 month. This would suggest that the implementation process is a key aspect of
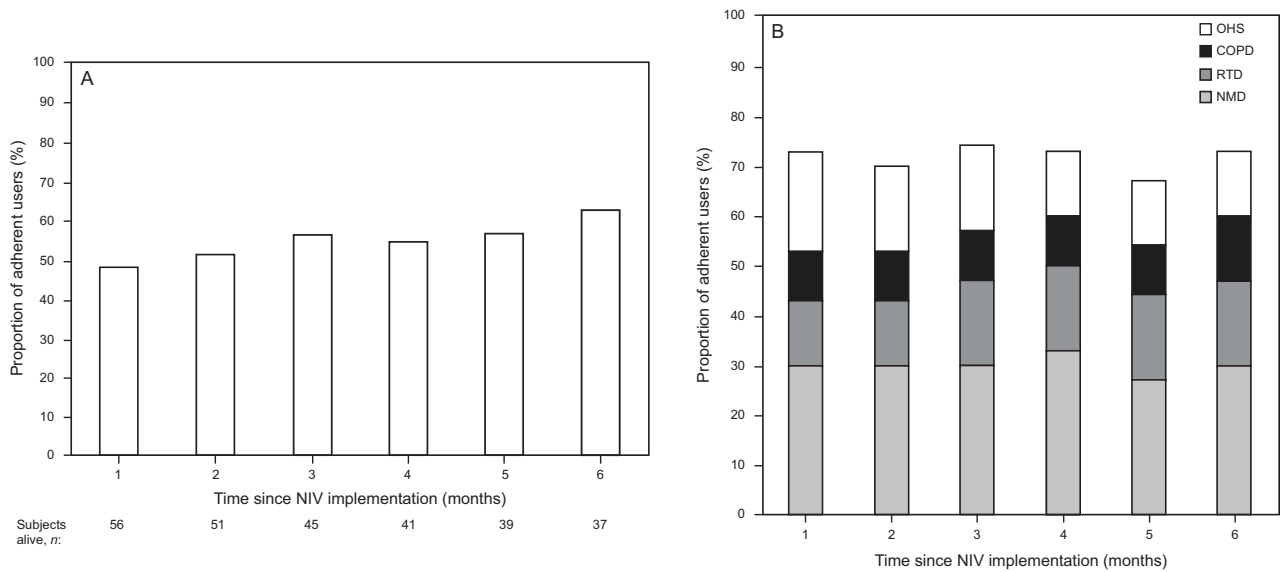
Fig. 2. Categorical adherence over 6 months in (A) subjects with motor neuron disease and (B) in subjects with stable or slowly progressive disease. NIV = noninvasive ventilation; OHS = obesity hypoventilation syndrome; RTD = restrictive thoracic disorders; NMD = other neuromuscular disease.

Table 4. Categorical Adherence Thresholds for NIV Usage at 6 Months or the Month Prior to Death

Average Daily NIV Usage at 6 Months or Prior to Death	PSG-Assisted Titration (n = 86)		In-Patient vs Out-Patient (n = 86)		In-Patient Admission Type (n = 24)		Residential Location (n = 86)	
	Yes (n = 55)	No (n = 31)	In-Patient (n = 24)	Out-Patient (n = 62)	Acute (n = 13)	Elective (n = 11)	Metropolitan (n = 60)	Regional (n = 26)
0–1 h	7 (13)	14 (45)	9 (38)	12 (19)	2 (15)	7 (64)	15 (25)	6 (23)
1–4 h	5 (9)	7 (23)	2 (8)	10 (16)	1 (8)	1 (9)	6 (10)	6 (23)
> 4 h*	43 (78)	10 (32)	13 (54)	40 (65)	10 (77)	3 (27)	39 (65)	14 (54)

Data are presented as n (%).
* > 4 h = adherent users
NIV = noninvasive ventilation
PSG = polysomnography

gaining durable improvements in adherence. What is uncertain is whether a single approach or a "one size fits all" intervention will be effective, or whether there are groups within these heterogeneous populations that are disadvantaged by burdensome care practices that may result in excess levels of nonadherence. Further exploration of the factors impacting adherence related to the individual (eg, disease, severity, symptoms, comorbidities), the device (eg, settings, titration method, interface), and the service (eg, access, support, method of implementation) are required to design better models of care that can more consistently result in better adherence. Robust reporting of adherence is required to achieve this.

We acknowledge that not all aspects of the model of care used by this HMV service would be acceptable to clinicians in other settings. For example, polysomnographic titration appears to be used infrequently elsewhere, and the evidence to support its routine use is limited.[1,24,43] In a pilot randomized controlled trial conducted by this research group, a supportive effect of polysomnographic titration of NIV on adherence was apparent in users who were initially nonadherent.[24] This finding requires replication in a larger multi-center study. Other investigators have described alternative models of care that could be effective at improving adherence but have infrequently subjected them to scrutiny within well-designed randomized controlled trials. Measures such multi-day inpatient admissions, home implementation, remote ventilator or physiological monitoring, auto-titration, and telemedicine strategies would all benefit from further supportive evidence to help optimize the care pathway for long-term users of NIV.

It remains uncertain which approach will prove most efficacious and cost-effective at improving NIV adherence.

Recent systematic reviews examining factors associated with effective initiation and adherence to NIV in patients with MND advocate for an individualized approach to respiratory management that is tailored to the differing needs of each patient.[12,44] This may include flexible service delivery models (eg, multidisciplinary teams, in-patient, out-patient, or home initiation), careful selection of interface and ventilation settings, adequate airway and secretion management strategies, and vigilant monitoring and adjustment of settings.[12,35] Recognizing that NIV can be a burdensome therapy for patients and their caregivers, patient-centered goals should be paramount. It is clear that a therapeutic gap exists within HMV populations, particularly among those with MND, and that this gap is difficult to bridge. Individuals with disorders such as MND deserve flexible, ethical, and effective treatment options, and the challenge for clinicians and researchers in this area is to come up with solutions that meet these goals.[42]

Our study has several limitations. This was an observational study at a single site, and, apart from MND, subject numbers from other disease groups were small. Results were not adjusted for individual diagnoses or subgroups (eg, MND phenotypes), gender, or location of care. No attempts were made to systematically record or explore the underlying reasons for low adherence when it was observed, and the strategies employed by clinicians to support adherence (eg, mask or setting changes, home visits, in-patient admissions) were not systematically examined in this work. This limits comparisons with other institutions that may employ different clinical approaches, management strategies, and techniques, and that manage different populations who are commencing long-term ventilation (eg, different proportions of individuals with COPD and OHS).[37] Nevertheless, this study of an unselected cohort provides a real-world illustration of the difference between average daily use and categorical adherence, and it highlights the importance of improved outcome reporting for both clinical practice and future research trials.

Conclusions

Adherence to NIV among new users at a single Australian HMV service was similar to that described in international settings. Those with MND had a lower categorical adherence rate than those with other stable or slowly progressive disorders. Additionally, adherence rates were lowest among those with MND who died within 6 months of starting NIV, highlighting this potential therapeutic target. Average daily use data appeared to conceal the degree of nonadherence to NIV. Reporting both categorical adherence rates (using a 4-h threshold) and average daily usage may improve transparency of outcomes in studies evaluating NIV and associated care practices.

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