ORIGINAL RESEARCH

Long-term survival following initiation of home non-invasive ventilation: a European study

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► Additional material is published online only. To view please visit the journal online (<http://dx.doi.org/10.1136/thoraxjnl-2019-214204>).

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Received 14 October 2019

Revised 25 May 2020

Accepted 26 May 2020

Published Online First

7 September 2020

ABSTRACT

Introduction Although home non-invasive ventilation (NIV) is increasingly used to manage patients with chronic ventilatory failure, there are limited data on the long-term outcome of these patients. Our aim was to report on home NIV populations and the long-term outcome from two European centres.

Methods Cohort analysis including all patients established on home NIV from two European centres between 2008 and 2014.

Results Home NIV was initiated in 1746 patients to treat chronic ventilatory failure caused by (1) obesity hypoventilation syndrome±obstructive sleep apnoea (OHS±OSA) (29.5%); (2) neuromuscular disease (NMD) (22.7%); and (3) obstructive airway diseases (OAD) (19.1%). Overall cohort median survival following NIV initiation was 6.6 years. Median survival varied by underlying aetiology of respiratory failure: rapidly progressive NMD 1.1 years, OAD 2.7 years, OHS±OSA >7 years and slowly progressive NMD >7 years. Multivariate analysis demonstrated higher mortality in patients with rapidly progressive NMD (HR 4.78, 95% CI 3.38 to 6.75), COPD (HR 2.25, 95% CI 1.64 to 3.10), age >60 years at initiation of home NIV (HR 2.41, 95% CI 1.92 to 3.02) and NIV initiation following an acute admission (HR 1.38, 95% CI 1.13 to 1.68). Factors associated with lower mortality were NIV adherence >4 hours per day (HR 0.64, 95% CI 0.51 to 0.79), OSA (HR 0.51, 95% CI 0.31 to 0.84) and female gender (HR 0.79, 95% CI 0.65 to 0.96).

Conclusion The mortality rate following initiation of home NIV is high but varies significantly according to underlying aetiology of respiratory failure. In patients with chronic respiratory failure, initiation of home NIV following an acute admission and low levels of NIV adherence are poor prognostic features and may be amenable to intervention.

INTRODUCTION

Home non-invasive ventilation (NIV) is widely used for the management of chronic hypercapnic respiratory failure in both Europe¹ and the USA.² While initially used in patients with chronic respiratory failure secondary to neuromuscular disease,³ there are increasing observational and randomised clinical trial data supporting the provision of home NIV in patients with obesity-related respiratory

Key messages**What is the key question?**

- What is the long-term outcome of patients treated with home non-invasive ventilation?

What is the bottom line?

- The median survival following initiation of home non-invasive ventilation is 6.6 years.
- Adherence to treatment (>4 hours per night) and elective timing of initiation of home non-invasive ventilation are possible modifiable factors associated with improved survival.

Why read on?

- This study describes home non-invasive ventilation populations at two large European home non-invasive ventilation centres and explores factors associated with mortality.

failure^{4 5} and COPD.^{6–8} These data, along with the increasing prevalence of obesity, have led to an expansion in the number of patients established on home NIV.^{9 10} However, unlike other chronic respiratory diseases such as idiopathic pulmonary fibrosis,¹¹ lung cancer¹² and pulmonary hypertension,¹³ the long-term outcome of patients with chronic hypercapnic respiratory failure treated with home NIV remains unclear. Previous data included patients receiving long-term oxygen and invasive ventilation¹⁴ and lacked generalisability due to the focus on a specific underlying respiratory disease from single centres.^{15–19} Furthermore, since previous data were published, NIV devices^{20 21} and set-up strategies^{22 23} have evolved, leading to significant changes in clinical practice. The aim of the current study was to report the underlying disease types for patients established on home NIV, the NIV device parameters and the long-term outcome from two European specialist centres.

METHODS

We conducted a cohort analysis of patients set up on home NIV in two specialist centres: one in France and one in the UK.

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To cite: Patout M, Lhuillier E, Kaltsakas G, et al. *Thorax* 2020;**75**:965–973.

Figure 1 Study population flow chart. CPAP, continuous positive airway pressure, NIV, non-invasive ventilation.

Population

Patients were prospectively included in administrative databases used for equipment-related purposes in two adult respiratory centres. Medical data and clinical outcome were retrospectively reviewed by selecting all patients who were newly established on home NIV between 2008 and 2014. We excluded all patients set up on CPAP, adaptive servo-ventilation and patients receiving invasive ventilation via tracheostomy. Decision to initiate home NIV was based on a comprehensive clinical and physiological assessment by a senior clinician with experience in home ventilation based on patient symptoms, arterial blood gas and lung function test results. Patient selection was in line with published guidelines, with NIV prescribed for patients with chronic hypercapnic respiratory failure and sleep disordered breathing. Patients with severe obstructive sleep apnoea and significant residual apnoea-hypopnoea index (>30 per hour) on maximal (20 cmH₂O) CPAP therapy or not tolerant of CPAP or hypercapnic despite CPAP therapy were also established on NIV. Home NIV was established at an inpatient assessment using respiratory polygraphy and/or overnight transcutaneous oximetry and/or morning arterial blood gas according to local established protocols. Overnight titration was performed to treat sleep disordered breathing and manage daytime chronic ventilatory failure. Based on clinical practice, patients were instructed to use their NIV for at least 4 hours per day, but ideally for the full duration of their sleep. Patients with progressive neuromuscular

disease were provided with devices with an internal battery and advised to extend use into wakefulness with disease progression.

NIV service

The characteristics of the NIV services and healthcare organisation are described in the online supplementary material.

Ventilator databases

For Rouen, the database was retrieved from ADIR Assistance (Asten Santé, Orvault, France), a healthcare provider that delivers home NIV for Rouen University Hospital. For London, the database was retrieved from Lane Fox Respiratory Service technical ventilator database, which records home NIV set-up for Guy's and St Thomas' NHS Foundation Trust. In both centres technical databases included patients' identification, date of birth, date of home NIV set-up, initial ventilator device and settings, interface, prescribed duration of ventilation, hours of NIV use (adherence), and date of last patient contact. Adherence to NIV was measured using the number of device's blowing hours divided by the number of days following NIV set-up. Changes in settings or interface were not systematically recorded and therefore were not included in the analysis. Patients were followed up until death or censored at the point of last verified health status or loss of contact with home ventilation centre. When applicable, date of cessation of follow-up from the NIV centre was recorded. Reasons for follow-up cessation

Table 1 Baseline demographics of the study population

	Total population (N=1746)	London population (n=1118)	Rouen population (n=628)	P value
Age (years)	60.5 (±15.9)	58.8 (±15.7)	63.6 (±15.8)	<0.001
Gender (male), n (%)	949 (54)	613 (55)	336 (54)	0.617
PaCO ₂ at admission for NIV set-up (kPa)*	7.1 (6.2–8.1)	7 (6.1–8.0)	7.5 (6.6–8.8)	<0.001
Spirometry at NIV set-up†				
FEV ₁ (L)	1.1 (0.7–1.6)	1.1 (0.7–1.7)	1.0 (0.7–1.4)	0.078
FVC (L)	1.7 (1.2–2.4)	1.7 (1.1–2.4)	1.9 (1.4–2.4)	<0.001
Underlying respiratory disease				0.007
Neuromuscular diseases, n (%)	397 (22.7)	290 (25.9)	107 (17)	<0.001
Motor neuron disease	144 (36.3)	84 (29)	60 (56.1)	<0.001
Duchenne muscular dystrophy	49 (12.3)	37 (12.8)	12 (11.2)	
Postpolio syndrome	40 (10.1)	39 (13.4)	1 (0.9)	
Myotonic dystrophy	27 (6.8)	19 (6.6)	8 (7.5)	
Spinal cord injury	24 (6)	14 (4.8)	10 (9.3)	
Diaphragm palsy	21 (5.3)	13 (4.5)	8 (7.5)	
Other neuromuscular conditions‡	92 (23.2)	84 (29)	8 (7/5)	
Obstructive airway diseases, n (%)	334 (19.1)	199 (17.8)	135 (21.5)	0.001
COPD	305 (91.3)	182 (91.5)	123 (91.1)	0.733
Bronchiectasis	14 (4.2)	8 (4)	6 (4.4)	
Asthma	10 (3.0)	5 (2.5)	5 (3.7)	
Other obstructive conditions‡	5 (1.5)	4 (2)	1 (0.7)	
Chest wall diseases, n (%)	95 (5.4)	59 (5.3)	36 (5.7)	0.714
Kyphoscoliosis	58 (61.1)	32 (53.3)	26 (72.2)	0.003
Scoliosis	15 (15.8)	15 (25.0)	0 (0)	
Post-tuberculosis	10 (10.5)	3 (5.0)	7 (19.4)	
Pneumonectomy	5 (5.3)	3 (5.0)	2 (5.6)	
Other restrictive conditions‡	7 (8.3)	7 (11.6)	1 (2.8)	
Obesity hypoventilation syndrome with or without obstructive sleep apnoea, n (%)	515 (29.5)	319 (28.5)	196 (31.2)	0.251
Obstructive sleep apnoea, n (%)	184 (10.5)	122 (10.9)	62 (9.9)	0.517
Overlap between obstructive airway disease and sleep apnoea, n (%)	221 (12.7)	129 (11.5)	92 (14.6)	0.072
COPD	206 (93.2)	122 (94.6)	84 (91.3)	0.588
Asthma	10 (4.5)	6 (4.7)	4 (4.3)	
Bronchiectasis	5 (2.3)	1 (0.8)	4 (4.3)	

Results are expressed in terms of mean and SD or median and IQR for continuous variable and in frequency for categorical values.

*n=1096.

†n=803.

‡Full list of other conditions can be found in online supplementary material.

COPD, Chronic obstructive pulmonary disease; NIV, non-invasive ventilation; PaCO₂, Partial pressure of carbon dioxide in arterial blood.

were classified as follows: (1) death; (2) non-adherence (<4 hours per night and clinical decision to withdraw therapy); (3) NIV no longer required; and (4) care transferred to another centre. Satisfactory adherence was defined as use >4 hours per day; however, NIV cessation was left to physicians' discretion.

Medical electronic record

Medical data were retrieved from the hospital electronic medical record by respiratory physicians using a standardised collection sheet (MP, EL, AB) who checked and confirmed their accuracy. Collected data were gender, underlying respiratory disease and timing of NIV set-up. Timing of NIV set-up was defined as follows: elective admission for stable patients referred for respiratory review that were subsequently established on home NIV and following an acute episode for patients admitted for decompensated respiratory failure and for which, after clinical stabilisation but before hospital discharge, transfer to a specialist centre for home NIV set-up was decided to be clinically necessary. Data from technical databases

were cross-checked with medical records and corrected accordingly. Based on the underlying pathology, patients were categorised into six different groups: neuromuscular disease (NMD), chest wall disease (CWD), obesity hypoventilation syndrome (OHS), obstructive sleep apnoea (OSA), obstructive airway diseases (OAD) or with an overlap between COPD and OSA (COPD-OSA overlap). For survival analysis, the NMD group was subdivided into rapidly progressive NMD (eg, motor neuron disease) or slowly progressive NMD (eg, Duchenne muscular dystrophy, myotonic dystrophy) (a full list of underlying neuromuscular disorders can be found in online supplementary eTable 1).

Statistical analysis

Continuous data are presented as mean and SD if normally distributed or median and IQR if non-normally distributed. Categorical data are presented as frequency counts and percentages. Comparisons were performed using Kruskal-Wallis test, χ^2 test, analysis of variance and Mann-Whitney test, as appropriate. Survival data were

Non-invasive ventilation

Table 2 Comparison of non-invasive ventilation set-up and setting between London and Rouen

	Total population (N=1746)	London population (n=1118)	Rouen population (n=628)	P value
NIV set-up following an acute respiratory failure (yes), n (%)	824 (48.6)	444 (53.9)	380 (60.5)	<0.001
Length of stay for NIV set-up following an acute respiratory failure	10 (5–18)	7 (3–17)	13 (9–18)	<0.001
Length of stay for NIV set-up following an elective admission	3 (2–4)	2 (2–3)	4 (3–4)	<0.001
Interface, n (%)				
Full face mask	1355 (77.6)	882 (78.9)	473 (75.3)	<0.001
Nasal mask	238 (13.6)	115 (10.3)	123 (19.6)	
Nasal pillows	64 (3.7)	33 (3)	31 (4.9)	
Total face mask	47 (2.7)	47 (4.2)	0 (0)	
Not available	42 (2.4)	41 (3.7)	1 (0.2)	
Life support NIV (yes)*, n (%)	609 (34.9)	515 (46.1)	94 (15)	<0.001
NIV mode, n (%)				
Pressure support	1405 (80.5)	859 (76.8)	546 (86.9)	<0.001
Pressure control	179 (10.3)	144 (12.9)	35 (5.6)	
Spontaneous	89 (5.1)	82 (7.3)	7 (1.1)	
Pressure support with target volume	40 (2.3)	11 (1)	29 (4.6)	
Not available	33 (1.9)	22 (2)	11 (1.8)	
Settings				
Positive inspiratory pressure (cmH ₂ O)	22±5	23±5	19±4	<0.001
Positive expiratory pressure (cmH ₂ O)	7±3	8±4	7±2	<0.001
Pressure support (cmH ₂ O)	14±5	15±5	12±3	<0.001
Backup rate (per minute)	13.2±2.5	13.4±2.8	12.8±1.6	<0.001
Additional oxygen (yes), n (%)	634 (36.3)	247 (22.1)	241 (38.4)	<0.001

Results are expressed in terms of mean and SD or median and IQR for continuous variable and in frequency for categorical values.

*Defined by a ventilator with built-in battery and approved for invasive ventilation.

NIV, non-invasive ventilation.

analysed using Kaplan-Meier method and log-rank tests. Patients for whom home NIV was withdrawn were censored at point of cessation of follow-up. Prognosis factors were analysed in univariate analysis and with a multivariate Cox model. For all tests, significance level was set at 0.05. Analyses were performed using SPSS V.23.0 and Prism V.6.0(h) for MacOS X (GraphPad Software, La Jolla, California, USA).

RESULTS

Diagnostic groups

Between 2008 and 2014, 1746 patients were established on home NIV, 1118 (64%) in London and 628 (36%) in Rouen (figure 1), with a median follow-up of 1.97 (0.78–3.78) years. Over the study period, the number of patients set up on home NIV increased by 5% per year, with 203 patients being set up in 2008 and 298 in 2014 (online supplementary eFigure 4). The baseline characteristics of the population are described in table 1. Patients set up in London were younger than patients set up in Rouen ($p=0.001$). The most frequent diagnostic category was OHS ($n=515$, 29.5%), followed by NMD ($n=397$, 22.7%), OAD ($n=334$, 19.1%) and COPD-OSA overlap ($n=221$, 12.7%). OSA and CWD were less frequent ($n=184$ (10.5%) and $n=95$ (5.4%), respectively). The distribution of diagnostic categories was different between the two centres ($p=0.007$). There were higher proportion of patients with NMD and lower proportion of patients with OAD in the London centre compared with Rouen ($p=0.001$).

Timing of NIV initiation and ventilator settings

Timing of NIV set-up (postacute and elective) and ventilator settings differed between centres. Patients with OAD were more likely to have their NIV set up following an acute admission (70%) than other groups of patients (NMD 42%, CWD 52%, OHS 49%, COPD-OSA 49% and OSA 22%; $p<0.001$).

The Rouen group had a higher proportion of NIV set-ups following an acute admission (60.5% vs 53.9%; $p<0.001$) and had a longer length of stay regardless of whether NIV was set up acutely or electively (elective admission for NIV set-up 2.0 days (2–4) ($p<0.001$) and non-elective admission 6.0 days (5–18) ($p<0.001$)). Ventilator device, mode, interface, pressure settings, backup rate and additional requirements varied between centres (table 2). The level of pressure support was significantly different over time ($p=0.0069$), with a higher pressure support in 2011 and 2012 when compared with 2008: 13.5 (11.0–17.0) and 14.0 (10.0–17.0) vs 13.0 (10.0–16.0) cmH₂O ($p=0.049$ and $p=0.002$, respectively). In each diagnostic group, ventilator settings used in the Rouen centre were lower than those used in London (figure 2). As part of the NIV set-up process supplementary oxygen was added to the ventilator circuit in 634 (36%) patients, with variation between diagnostic groups (OAD 64%, COPD-OSA overlap 49%, OHS 37%, CWD 33%, OSA 27% and NMD 10%; $p<0.0001$).

NIV adherence

NIV adherence to treatment was higher in Rouen than in London (7.6 ± 4.6 hours/day vs 5.5 ± 3.6 hours/day; $p<0.001$). NIV

Figure 2 Comparison of NIV settings and adherence per day between London and Rouen according to diagnostic group. (A) Comparison of positive inspiratory pressure used. (B) Comparison of positive expiratory pressure used. (C) Comparison of backup rate used. (D) Comparison of adherence. Box with lines: London patients; coloured box: Rouen patients. Yellow: NMD; light red: CWD; blue: OAD; green: overlap; red: OHS; grey-green: OSA. **P<0.001; ns, not significant. CWD, chest wall disease; EPAP, expiratory positive airway pressure; IPAP, inspiratory positive airway pressure; NIV, non-invasive ventilation; NMD, neuromuscular disease; OAD, obstructive airway disease; OHS, obesity hypoventilation syndrome; OSA, obstructive sleep apnoea; overlap, overlap between OAD and OSA.

adherence varied according to the underlying diagnostic group (NMD 7.1 (4.0–9.5) hours/day; CWD 7.5 (4.1–9.3) hours/day; OAD 6.5 (3.7–8.7) hours/day; OHS 5.8 (3.0–7.8) hours/day; and OSA 5.5 (2.1–7.0) hours/day; $p<0.001$). NIV adherence was higher in all diagnostic categories in the Rouen group, with the exception of the NMD category (figure 2).

Survival

Following NIV initiation, overall survival was 6.63 years. Survival at 1 year, 3 years and 5 years was 85.9% (95% CI 83.2 to 86.6), 68.7% (95% CI 66.0 to 71.2) and 58.3% (95% CI 55.0 to 61.5), respectively, with a difference observed between the diagnostic categories ($p<0.001$). Survival was 1.0 (95% CI 0.7 to 1.2) year in the rapidly progressive NMD category, 6.3 years in the CWD category, 2.7 (95% CI 2.2 to 3.2) years in the OAD category, and 6.6 years in the COPD-OSA overlap category. Median survival was not reached in the slowly progressive NMD, OHS and OSA groups (figure 3). In an univariate analysis, the centre of NIV initiation did not have any impact on mortality ($p=0.358$), whereas age >60 years ($p<0.001$) and having NIV set up following an episode of acute respiratory failure ($p<0.001$) were both associated with higher mortality. In a multivariate analysis, age, gender, timing of NIV set-up and underlying disease were significantly associated with survival (table 3). Analysis of the cohort with removal of rapidly progressive NMD did not impact on the variables associated with prognosis (online supplementary eTable 2).

NIV cessation

During the observation period, 680 patients discontinued the home NIV programme. The reasons for cessation included death (503 patients, 74%), NIV withdrawal due to poor adherence (100, 15%), reversal of chronic ventilatory failure and treatment cessation (42, 6%), and transfer to another centre (35, 5%).

There was no difference in distribution of follow-up outcomes between centres ($p=0.209$).

DISCUSSION

These data represent the largest long-term outcome data of patients initiated on home NIV for treatment of chronic ventilatory failure. The overall 5-year survival following initiation of home NIV was poor at 58%; however, outcome varied according to the aetiology of respiratory failure, timing of NIV initiation, gender and age at initiation of home NIV. A clinical approach to improving NIV adherence and elective timing of initiation of home NIV may enhance outcome.

Survival outcome

The 1-year and 5-year survival of patients initiated on home NIV are 86% and 58%, respectively, which are worse than patients receiving therapy for idiopathic pulmonary fibrosis (1-year survival of 97%)²⁴ or pulmonary hypertension (5-year survival of 57%).¹³ As expected, survival varied depending on the underlying aetiology of chronic ventilatory failure. Patients with rapidly progressive NMD had a survival similar to previous published data.³ Patients with COPD had a similar survival to patients in the fourth quartile of the BODE (body mass index, airflow obstruction, dyspnoea and exercise capacity) index,²⁵ and therefore initiation of home NIV should trigger evaluation for lung transplantation or palliative care referral if lung transplantation is not appropriate.²⁶

Clinical implications

An important finding of the current study is the identification of two potentially modifiable factors associated with improved survival following initiation of home NIV. First, we have shown

Figure 3 Survival curve after set-up of home non-invasive ventilation depending on underlying disease. Rapidly progressive neuromuscular disease group (rapid NMD: continuous blue), slowly progressive neuromuscular disease group (slow NMD: dashed blue), obstructive airway disease group (OAD: continuous black), overlap between COPD and OSA group (COPD-OSA: dashed black), chest wall disease group (CWD: light green), obesity hypoventilation syndrome group (OHS: continuous red) and obstructive sleep apnoea group (OSA: dashed red).

Table 3 Factors associated with mortality in univariate analysis (log-rank) and multivariate analysis (Cox regression)

	Univariate analysis (log-rank)		Multivariate analysis (Cox regression)	
	HR (95% CI)	P value	HR (95% CI)	P value
NIV centre (reference: Rouen)				
London	0.903 (0.756 to 1.079)	0.358	0.944 (0.778 to 1.145)	0.560
Gender (reference: male)				
Female	0.890 (0.749 to 1.058)	0.098	0.790 (0.652 to 0.959)	0.017
Age (reference: below 60 years old)				
Above 60 years old	3.131 (2.336 to 3.297)	<0.001	2.398 (1.912 to 3.008)	<0.001
Underlying respiratory disease (reference: overlap between obstructive airway disease and obstructive sleep apnoea)				
Rapidly progressive neuromuscular disease	4.349 (4.095 to 7.906)	<0.001	4.860 (3.432 to 6.881)	<0.001
Slowly progressive neuromuscular disease	0.655 (0.442 to 0.977)	0.038	0.852 (0.550 to 1.320)	0.474
Obstructive airway disease	2.475 (1.771 to 2.988)	<0.001	2.233 (1.623 to 3.073)	<0.001
Chest wall disease	1.016 (0.639 to 1.616)	0.0946	1.169 (0.723 to 1.891)	0.524
Obesity hypoventilation syndrome with or without obstructive sleep apnoea	0.633 (0.426 to 0.867)	0.006	0.721 (0.509 to 1.022)	0.066
Obstructive sleep apnoea	0.469 (0.318 to 0.748)	0.001	0.516 (0.315 to 0.844)	0.008
Timing of NIV set-up (reference: elective set-up)				
Set-up following an acute event	1.860 (1.545 to 2.203)	<0.001	1.376 (1.161 to 1.731)	0.001
Adherence (reference: below 4 hours per night)				
Adherence above 4 hours per night	1.110 (0.903 to 1.376)	0.315	0.636 (0.512 to 0.790)	<0.001

NIV, non-invasive ventilation.

that NIV initiation following an episode of acute decompensated hypercapnic respiratory failure was associated with an increase in mortality. It can be postulated that patients presenting with decompensated respiratory failure would be further through the natural history of the disease and thus would be expected to have a higher mortality. Hence, early detection by screening may produce a lead time bias. However, data from patients with rapidly progressive NMD suggest that early initiation of NIV may improve the survival of these patients.^{27 28} An acute exacerbation of respiratory failure can cause further lung injury²⁹ and therefore lead to worse outcomes. Although we still lack early predictors of the onset of chronic respiratory failure, it can be speculated that close monitoring of patients at high risk of chronic hypercapnia would allow for earlier intervention and may therefore influence long-term outcomes. Similarly to most centres, such an approach was already established in our centres for patients with NMD with 3-monthly multidisciplinary follow-up. Such management could be extended to at-risk patients with OSA and COPD. However, there are no data with sufficient accuracy to provide reliable screening tools to predict early respiratory failure^{30–32} or evidence that such strategies are cost-effective.

Second, we have shown that an adherence to home NIV of greater than 4 hours per night was associated with an improved survival. To the best of our knowledge, our results are the first to show a correlation between adherence and mortality independent of the underlying disease. Interestingly, the cut-off of 4 hours of home NIV use per night was based on routine clinical practice, and studies in patients with eucapnic OSA treated with CPAP with this level of adherence leading to improvements in excessive daytime somnolence but not survival.^{33–35} Our results support the use of a 4 hours per night target for minimal adherence in all patients with chronic ventilatory failure set up on home NIV, irrespective of underlying disease. However, in patients with advanced disease, adherence can be associated with a worse prognosis as increased use may reflect worsening respiratory failure. Interventions that can facilitate patient home NIV adherence, such as telemonitoring,³⁵ may have an impact on long-term outcome and should be the focus of future work. Better adjustments of ventilator settings may also contribute to improve adherence,³⁶ although such approach may need to be limited to a well-defined subgroup of patients,³⁷ as the use of polysomnography during NIV set-up remains controversial³⁸ and the lack of clear clinical efficacy is further impaired by practical constraints of delivering a high-cost low-availability intervention such as polysomnography.

Comparison with previous studies

Despite an increase in the total number of patients using home NIV,² few data exist reporting long-term mortality. The only detailed data set previously reported was based on historical data and included patients on long-term oxygen therapy, and thus its relevance to the current population of home ventilation users is limited.¹⁴ Indeed, in this previous cohort the median survival of patients with 'chronic bronchitis' was 3 years. Interestingly, this reported survival is comparable with the current data in the OAD patient category, indicating little improvement in outcome in this patient group despite changes in pharmacotherapy and supportive care made over the last 20 years. Comparison with the study reported by Chailleux *et al*¹⁴ highlights the demographic change in home NIV. Chronic ventilatory failure, secondary to tuberculosis or poliomyelitis, is increasingly uncommon. The current data demonstrated that obesity-related respiratory failure (OSA and/or OHS) represents the most frequent indication for home NIV initiation.⁹ The use of CPAP may be considered as an alternative to NIV³⁹; however, in our

cohort, the 3-year survival was slightly lower than that published by Masa and colleagues (82% vs 89%).⁴⁰ This could be explained by the fact that our population was unselected and that patients were frequently established after acute respiratory failure who were excluded in the Pickwick study. For patients with OAD, Köhnlein *et al*⁷ have reported a mortality rate of 10% at 1 year in patients established on home NIV. In our data, mortality rate for patients with OAD was 25% at 12 months. The higher mortality seen in our data likely reflects that the patients recruited into the study by Köhnlein and colleagues⁷ required clinical stability, whereas clinical practice at the two centres was to initiate the majority of home NIV in OAD following an acute exacerbation, with a published mortality in this group in excess of 25% in recent clinical trials.^{6 41}

For patients with rapidly progressive NMD, we found a median survival rate of 1 year higher than that obtained in the initial randomised controlled trial in this group of patients.³ Similar to the other diagnostic groups the clinical population was more heterogeneous than the trial population. Our median survival is lower than that reported by Berlowitz *et al*.⁴² Again, this is likely to be explained by the significant proportion of patient set-ups occurring after an acute event in our data.

Increasing demand for home NIV

In the current study, the increase in NIV set-up was 5% per annum. This growth has been described in France¹⁰ and is explained by the increasing burden of obesity^{43 44} and obesity-related respiratory failure, with this diagnostic category now representing the most common indication for home NIV set-up. Changes in home NIV set-up for COPD may have been influenced by the results of two recent randomised clinical trials demonstrating the benefit of home NIV both in the chronic stable and postacute state.^{6 7} These data have been included in both national and international guidance,^{45–47} and it is expected that this would increase the referrals for home NIV in this patient group.

COPD-OSA overlap

Patients with COPD-OSA overlap syndrome have been shown to have significantly worse outcomes than patients with COPD alone.⁴⁸ However, these data are not confined to patients with respiratory failure. In the data reported here patients with respiratory failure caused by COPD-OSA overlap have an outcome that is between that of those patients with either obesity-related respiratory failure or COPD alone. The provision of positive airway pressure therapy has been shown to improve outcomes in patients with COPD-OSA, although the benefit on mortality may be confined to patients with hypercapnia.^{48 49} These data support the screening of patients with COPD-OSA overlap for the presence of hypercapnia to allow consideration of initiation or transition to NIV and provide an insight for future clinical trials comparing NIV with CPAP in this patient population.

Difference between the home NIV centres

This study compared two specialist home NIV centres, with different models of NIV management and integration with local healthcare organisations, although both university hospitals in urban areas. The data demonstrate variation in clinical practice between centres. Indeed, in Rouen, more patients were set up following an acute event. This can be explained by the fact that the London centre is a tertiary referral centre, whereas Rouen is a secondary care hospital. The London centre established significantly more patients on NIV in the study period as it covers a larger geographical area with more inhabitants than Rouen. Ventilator settings also varied between the centres, with the London centre using higher average ventilator

pressures than the Rouen. However, the level of pressure per se is not a marker of efficacy. Indeed, patients in London were significantly younger suggesting a more severe disease and the proportion of overweight patients was higher in England than in France, which may impact on ventilatory requirement. In both centres, NIV was titrated in order to target significant CO₂ reduction measured with nocturnal transcutaneous CO₂ monitoring or evening-morning arterial blood gas. The similar long-term survival in both centres suggests adequate ventilator set-up despite the variation in pressures delivered. Further titration during follow-up may have minimised this difference. This difference in the level of pressure may explain why a higher proportion of full face masks were used in London. However, in the combined population the proportion of full face masks is similar to that previously reported.⁵⁰

Despite a higher home NIV adherence in Rouen, there was not an associated difference in mortality. This discrepancy may be explained by different factors. First, the lower pressures used to establish home NIV in Rouen may enhance comfort and tolerance; however, lessons learnt from COPD trials and in NMD⁵¹ emphasise the need for a control of respiratory failure to achieve clinical benefits. Second, a longer length of stay during set-up in Rouen may allow more time for training and education, improving adherence. Finally, the structure of the respective healthcare organisations⁵² may be responsible, with home follow-up by an external healthcare provider (ADIR Assistance) being used in Rouen, whereas London patients had hospital-based follow-up. Longer contact time and home visits may have facilitated greater patient understanding of the technique and treatment, promoting greater adherence. The organisation of home care delivery for respiratory failure treatment in France relies on external care providers that have to comply with strict legal obligations. No study has demonstrated the cost-effectiveness of this approach.

Limitations of the study

Inherent to the study design there are missing data and data that were not possible to validate in the medical record. However, we carefully chose the data to include variables that were prospectively routinely collected in the clinical record to maximise integrity. This has led to one of the main limitations of the current study, which is the missing physiological data, in particular the baseline arterial blood gas measurement and spirometric data, as well as the arterial blood gas data after home NIV set-up. As these data were not always prospectively gathered, they were not included in the analysis for long-term outcome. Moreover, a significant proportion of patients were initiated on home NIV following an acute episode of decompensated acute on chronic ventilatory failure. As they were treated with acute NIV, no arterial blood gas value in the stable state was available. As we assessed adherence to NIV since NIV set-up, we were not able to analyse change in adherence over time that may be a better survival predictor especially in rapidly progressing disease. As we assessed adherence to NIV since NIV set-up, we were not able to analyse change in adherence over time that may signify end-stage disease in rapidly progressing disease. Finally, we did not collect changes in NIV settings during follow-up. These changes may reflect disease progression and may also act as a useful prognostic marker.

CONCLUSION

These data represent the largest long-term outcome data of patients initiated on home NIV for the treatment of chronic ventilatory failure. The 5-year survival following initiation of home NIV was almost 60%, with aetiology of respiratory failure, gender and age at initiation as key determinants of

long-term survival. Potentially modifiable factors impacting on survival were NIV adherence and elective set-up of home NIV. Our results highlight the importance of organising dedicated pathways for patients with chronic respiratory failure in order to identify patients earlier and to provide adequate follow-up after NIV initiation in order to maximise adherence to treatment.

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Funding JS' contributions were partially supported by the National Institute for Health Research (NIHR) Biomedical Research Centre based at Guy's and St Thomas' NHS Foundation Trust and King's College London, UK. The views expressed are those of the authors and not necessarily those of the NHS, the NIHR or the Department of Health.

Competing interests MP reports personal fees from ResMed, grants and non-financial support from Fisher & Paykel, non-financial support from MSD, non-financial support and personal fees from Asten, grants from ADIR Association, grants from B&D Electromedical, personal fees from Philips Respironics, and personal fees and non-financial support from Chiesi, outside the submitted work. EL reports non-financial support from Asten, outside the submitted work. JD is an employee of Asten. AD reports grants from Philips Respironics, outside the submitted work. NH reports grants from Guy's and St Thomas' Charity, during the conduct of the study, grants from Philips Respironics, non-financial support from Philips Respironics RT Meeting (MYOTRACE), personal fees from Fisher & Paykel, grants from ResMed, grants from B&D Electromedical, and grants from Fisher & Paykel, outside the submitted work. In addition, NH has a patent MYOTRACE pending and is on the Pulmonary Research Advisory Board for Philips. NH's research group has received unrestricted grants (managed by Guy's and St Thomas' Foundation Trust) from Philips Respironics, Philips, ResMed, Fisher & Paykel and B&D Electromedical. Philips Respironics is contributing to the development of the MYOTRACE technology. PBM reports grants and personal fees from Philips Respironics, grants and personal fees from ResMed, and grants and personal fees from B&D Electromedical, outside the submitted work. GK, PL-D, AB, MR, GA, PM, L-CM, CV, JS, JFM and AC have nothing to disclose.

Patient consent for publication Not required.

Ethics approval The study was approved by the local ethic committee of Rouen University Hospital, France (#E2017-21) and registered as a service evaluation at Guy's and St Thomas' NHS Trust, London, UK (#7511).

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement Data will be available upon reasonable request to the corresponding author.

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