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Time-to-death in chronic respiratory failure on home mechanical ventilation: a cohort study

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Short title: Death on home mechanical ventilation.

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ABSTRACT

Background and objective: Home mechanical ventilation (HMV) is used in heterogeneous conditions underlying chronic hypercapnic respiratory failure, but there are sparse data on long-term clinical outcomes. The aim was to systematically analyse the time and the circumstances of death on HMV.

Methods: All-cause mortality data of HMV patients were prospectively collected between 2008 and 2018 in a large tertiary centre. Data were categorised into diagnostic groups including neuromuscular disease (NMD), chest wall disease (CWD), chronic obstructive pulmonary disease (COPD), obesity hypoventilation syndrome (OHS), overlap syndrome of COPD and OSA (overlap) and other group. The primary outcome was time-to-death from initiation of HMV.

Results: 1,210 deaths were recorded over a 10-year period. Median time-to-death was 19.5 [6-55] months and differed between groups (Kruskal Wallis $p<0.001$). CWD (98.5 [23.5-120] months) and slowly progressive NMD (64.5 [28-120] months) had the longest time-to-death on HMV, while OHS (33 [13-75] months) and overlap syndrome (30.5 [14.5-68.5] months) had a longer median time-to-death than COPD (19.5 [7-42.5] months) and motor neurone disease (7 [3-14] months). Daily adherence to HMV of greater than 4 hours/night was associated with better outcomes (10 [3-24] vs. 30 [10-76] months; $p<0.001$). 43% with confirmed location of death died outside the hospital.

Conclusions: The time-to-death on home mechanical ventilation varies widely across disease groups with chronic respiratory failure and seems to be associated with daily usage time.

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INTRODUCTION

Chronic respiratory failure is associated with high morbidity and adverse pathophysiological sequelae, and may be a life-limiting factor in prevalent diseases such as chronic obstructive pulmonary disease (COPD), obesity hypoventilation syndrome (OHS), overlap syndrome of COPD and obstructive sleep apnoea (OSA), and neuromuscular disease (NMD) or chest wall disease (CWD). Chronic hypercapnic respiratory failure can effectively be treated with long-term positive pressure ventilation, which is either applied non-invasively via an interface such as a mask or invasively via tracheostomy – each type of ventilation having its advantages and drawbacks. According to the underlying pathology and ventilator dependency, ventilation is used during sleep or often additionally during wakefulness (intermittently or up to 24 hours a day). Positive pressure ventilation is an indefinite treatment in chronic respiratory failure, and it is preferentially provided in the community as home mechanical ventilation (HMV). HMV is defined as either daily ventilation outside the hospital for more than three months. Successful initiation and long-term care of patients on HMV requires specialist services, and HMV is a growing area within respiratory medicine. In recent years, HMV is increasingly used [1, 2] to treat chronic ventilatory failure in different underlying conditions and has been shown to improve quality of life and prolong survival in different patient groups.[3, 4] Although evidence from randomised controlled trials is limited [5-7], the beneficial effect of HMV on long-term outcomes has been established for restrictive chest wall and slowly progressive neuromuscular diseases, where respiratory failure is the most common cause of death.[3] However, the spectrum of diseases resulting in chronic respiratory failure is changing. The prevalence of Post-Polio Syndrome has decreased while COPD and OHS are more common indications for HMV in chronic respiratory failure nowadays. There is mounting evidence of efficacy and improved survival and quality of life in these patient groups.[5, 6, 8, 9] However, outcomes of HMV may differ due to various factors, including progression of the disease, other organ failures and comorbidities. Little is known on long-term outcomes and the role of daily usage of HMV. The aim of this study was to compare time on HMV until death in different disease key groups in a large cohort of patients with chronic respiratory failure as well as to elucidate HMV usage patterns and the circumstances of end of life of these patients.

PATIENTS & METHODS

Design and study population

Data on all-cause mortality of all patients on HMV treated in one of the largest weaning and home ventilation services in the UK (currently treating more than 2,300 patients on HMV) were systematically and prospectively collected in a database since 2008, checked and analysed for the period from 01/01/2008 to 30/11/2018. All adult patients (age ≥18 years) established on HMV to treat chronic hypercapnic respiratory failure (p_aCO2 > 6 kPa or > 45 mmHg) and having died between 2008 and 2018 were eligible. Data collection for all-cause mortality involved screening of the electronic patient records of the unit and hospital, by contacting the patient's family or their general practitioner or respiratory physician responsible for follow-up as well as consulting the UK death register. Mortality cases are regularly reviewed within multi-disciplinary mortality meetings to learn from events and conclude whether this was an expected or unexpected outcome. This study complies with the Declaration of Helsinki of the World Medical Association and ICH-GCP-Guidelines. The study was approved by the institutional review board (Guy's and St Thomas' NHS Foundation Trust, project number 2017/7511) and registered on the Research Registry (Oxford, UK; researchregistry.com; UIN: researchregistry4122).

Outcomes

The primary outcome was the median time-to-death (months) on HMV within the following key groups with chronic respiratory failure:

1) Slowly progressive neuromuscular disease (NMD), e.g. muscular dystrophy type Duchenne
2) Rapidly progressive NMD, mainly motor neurone disease
3) Chest wall disease (CWD)
4) Chronic obstructive pulmonary disease (COPD),
5) Obesity hypoventilation syndrome (OHS),
6) Overlap syndrome of COPD and OSA (OVERLAP) and
7) Other (OTHER), e.g. traumatic spinal cord injury.

Kaplan Meier estimates of time-to-death on HMV were compared between these key groups. NMD and CWD is a heterogeneous group and additional subgroup analysis was performed (rapid

progressive NMD like motor neurone disease/MND, slowly progressive NMD like muscular dystrophy type Duchenne and other myopathies, and CWD).

Additional outcomes were differences between invasively and non-invasively ventilated patients, the location of death (home *vs* hospice *vs* hospital), the cause and assessment of death (respiratory *vs* non-respiratory, expected *vs* unexpected), the daily usage of HMV, and where available pulmonary function tests and arterial blood gases (e.g. pulmonary function test not available in tracheotomised patients; latest documented measure used).

Statistics

Data were tested for normality distribution using the Shapiro-Wilk and Kolmogorov-Smirnov tests. Data are described as mean (standard deviation, SD) or median (interquartile range, IQR; 1^{st} – 3^{rd} quartile) depending on their distribution. Baseline characteristics were compared by Pearson's Chi-square test (categorical variables) and ANOVA (analysis of variance) or Kruskal-Wallis equality-of-populations rank test, respectively. Kaplan Meier curves were used to visualise time-to-death (time on HMV until death) and outcomes were compared between groups using Kruskal-Wallis rank test (overall) and Mann Whitney U tests (pairwise). Multivariate linear regression analysis with analysis of residuals was used to study the association of daily usage of HMV with the time-to-death. Statistical significance level was set to alpha < 0.05. Analyses were performed with Stata version 15.0 (StataCorp, College Station, TX/USA).

RESULTS

Study population

Within a decade, 1,210 deaths on HMV were documented. The most prevalent key group were patients with NMD and CWD (n=533 [44%]), followed by COPD (n=296 [24%]), OHS (n=202 [17%]) and OTHER (n=127 [11%]). Patients with COPD-OSA-Overlap Syndrome constituted the smallest group (n=52 [4%]) (**table 1**). Subgroups within the key groups are provided in the online supplement (**E-table 1-2**). Overall, 88% of the patients were established on non-invasive ventilation and 12% were ventilated invasively via tracheostomy (**E-table 3**). Patients within the NMD and CWD and OTHER group were younger at the time of death than those in the COPD and OVERLAP group ($p < 0.005$ for all comparisons). The majority of patients were ventilated with pressure support (PSV, 62%) or pressure controlled (PCV, 34%) ventilation. However, the modes of ventilation differed between key groups (**table 1**), e.g. most patients with COPD or OHS were set-up on PSV whereas half of patients with NMD were set up on PCV. The mean inspiratory positive airway pressure (IPAP) across all groups was 21.9 cmH_2O and the mean expiratory positive airway pressure (EPAP) 6.6 cmH_2O, with a higher pressure support in COPD ($p < 0.001$) and a significantly higher EPAP in OHS and OVERLAP (**table 1**, $p < 0.001$). More than half of patients with COPD and a quarter of those with OHS used additional long-term oxygen therapy (LTOT), whereas only a minority of patients with NMD and CWD or in the OTHER group were established on LTOT. Hours of usage of HMV differed significantly between the key groups but was overall above the empirically used threshold of 4 hours/day in all groups (**table 1**). The latest documented mean (SD) p_aCO_2 (n=890) was 7.0 (3.0) kPa, and the mean (SD) p_aO_2 (n=674) was 8.9 (2.1) kPa. Mean (SD) FEV_1 (n=591) was 0.9 (0.5) l and FVC (n=584) was 1.4 (1.0) l.

Time-to-death (primary outcome)

The median time-to-death was 19.5 (6-55) months but differed significantly between groups (**figure 1, table 2, E-table 4**). It was longest for those with CWD or slowly progressive NMD (myopathy) and longer for OHS and OVERLAP than for COPD, OTHER or rapidly progressive NMD (**E-table 4**).
In the subgroups of NMD and CWD, patients with CWD or myopathies had a longer time-to-death than patients with motor neurone disease (MND) (**table 2, figure 2**).

Compliance with HMV

The mean daily usage of HMV (n = 1143, mean ± SD 9.6 ± 7.7 h) significantly differed across key groups (OTHER > NMD and CWD > COPD/OHS/OVERLAP, see **table 1**). Overall, 15% of patients were 24h-ventilator-dependent (one quarter of those was on non-invasive and three quarters were on invasive HMV) and 26% used HMV for >12 hours. The largest proportion of patients were ventilated between 4-12 hours (46%), and 22% of patients used their HMV < 4 hours/day (non-compliant, 7% used it not at all).

Location and cause of death

The location of death was unknown in 21%; 34% died outside the hospital (20% at home, 14% in a hospice), whereas 45% of patients on HMV died in a hospital (see **E-table 5**). 43% with confirmed location of death died outside the hospital. The proportion of patients dying at home or in a hospice was highest (55%) in the subgroup of patients with motor neurone disease. Death was classified as expected by the treating team in 45% and as unexpected in 33%; no judgement was possible in 22%. Death was categorised as respiratory-related in 30% and non-respiratory-related in 25%, and 45% of cases were unclassifiable from the data available.

Comparison non-invasive *vs* invasive HMV

Time-to-death did not differ significantly between patients treated with NIV and invasive HMV (p=0.37) (**E-figure 1**). Invasive HMV was mainly provided to those patients in the OTHER group (mainly traumatic spinal cord injuries) or NMD and CWD group, each representing almost half of patients with tracheostomy; the group OTHER constituted only 6% of patients on NIV. Patients with NMD and CWD were the most prevalent key group for both non-invasive and invasive HMV (see **E-table 3**). Ventilation modes (more PCV than PSV in the invasive group, 64% *vs* 30%, p<0.001) and the proportion of patients with LTOT (NIV > invasive, p=0.02) differed between groups. Invasively ventilated patients had significantly longer daily usage of HMV when compared to NIV (23.2±3.0 vs 7.5±5.9 hours/day, p<0.001) (**E-table 3**).

Comparison of the subgroups of NMD and CWD

Patients with MND or CWD were older than those with myopathies or neuropathies (see **E-table 2**). Median time-to-death varied substantially (**figure 1**): Patients with MND or neuropathy lived less than

one year on HMV whereas patients with stable CWD or myopathy used HMV for several years until the end of life (see **E-table 2**).

Effect of usage of HMV

Daily usage of HMV within the non-24h-ventilator-dependent was associated with time-to-death on HMV (beta 0.28, p<0.001, **E-table 6**), even when correcting for age, gender and key group. There was a significant longer time-to-death for patients using NIV for more than 4h/day compared to those who used NIV for shorter periods (p<0.001) (**E-table 6, figure 2**). Whereas the group using HMV for less than 4h per day consistently had a shorter time on HMV until death compared to all other compliance groups using 4-hour-blocks/day, the groups using HMV 8-<12h, 12-<16h and 16-<20h did not differ significantly in their time-to-death HMV but still had a significant longer time-to-death in comparison to those using HMV less than 4h or those that were 24h-ventilator dependent (**E-table 7-8, figure 2, E-figure 2**). The NMD group had the same pattern of effect of usage hours per day as the whole cohort with the exception that being ventilator-dependent for >16h was associated with a shorter time-to-death (**E-figure 3**). In the COPD cohort, longer daily usage of HMV was gradually associated with a longer time-to death up to 20h usage (**E-figure 4**).

DISCUSSION

This large cohort study of patients on HMV demonstrates that the time-to-death on HMV varies widely from less than one year to many years across different disease groups with chronic respiratory failure and suggests an association of the time-to-death with HMV usage. The evolving discipline of HMV accumulates evidence of survival benefit in highly prevalent diseases such as COPD and OHS, but long-term outcomes still warrant further data to understand the added value of HMV. The time-to-death is around five years in patients with CWD and slowly progressive NMD, around two to three years in those with OHS and Overlap Syndrome, around one to two years in COPD patients and those with other diseases that lead to chronic hypercapnic respiratory failure. It is less than one year in patients with motor neurone disease. However, long-term survivors can be found in all groups and this is not reflected in this cohort of deceased patients.

It is of interest that the time-to-death did not differ between deceased patients on non-invasive and tracheostomy ventilation. When considering only patients not being ventilator-dependent for 24 hours,

longer daily usage of HMV was associated with a longer time-to-death. An experience-based cut-off of a daily usage of >4hours of HMV was associated with longer time-to-death compared to those with lower adherence. At least one third of patients on HMV died outside the hospital, but the majority of patients did not.

Clinical Significance

This is the largest report on mortality in different patient groups on HMV. In another large cohort study on HMV investigating long-term outcomes in motor neurone disease in comparison to other key groups, survival of patients with motor neurone disease was similar to our data, but patients with COPD had a longer survival[4], which reflects the different methodologies of studying outcomes (survival *vs* mortality database). However, the current data are comparable to survival data of patients newly set-up on HMV, which showed a median survival on HMV of several years but differed depending on the disease groups. In accordance with our finding, usage of HMV for >4hours/day was associated with better survival.[10] Compared to previous data, the proportion of patients with COPD and motor neurone disease using HMV has increased.[3] Our data suggest that HMV supports stable management of hypercapnic respiratory failure in patients with CWD or slowly progressive NMD, such as Duchenne muscular dystrophy, for many years, whereas time-to-death is only a few months in motor neurone disease despite the use of HMV. However, symptom relief, control of breathlessness and improvement of quality of life are thought to be important outcomes in this cohort as well. In addition, the time-to-death in different disease groups would need to be compared to the expected survival and progression without using HMV.

The use of HMV in the management of patients with slowly progressive NMD and CWD has dramatically increased time-to-death in recent decades.[11, 12] A survival benefit has also been shown in other key groups.[5, 8, 13-16] The rapidly increasing prevalence of obesity with patients who develop hypercapnic respiratory failure (OHS) frequently affects young patients, and long-term NIV has been shown to improve health-related quality of life, survival and reduce complications and hospitalisations in these patients. Therefore, HMV potentially has a relevant effect on long-term outcomes and health care burden in these patients. Why patients with Overlap Syndrome seem to have more favourable outcomes than patients with COPD remains unclear (pulmonary mechanics,

intermittent hypoxia, earlier symptomatic presentation in the sleep laboratory) but might be influenced by differences in severity of COPD and additional symptoms, leading to a selection bias.

Pressure settings in this cohort revealed a trend towards high-intensity ventilation in COPD, but did not differ between the first (2008-2012) and the second half (2013-2018) of the analysed period (considering recent evidence of beneficial effects of high-intensity NIV).[5, 17] Although non-invasive positive pressure ventilation has been used in patients with extra-pulmonary restrictive ventilatory disorders for more than 30 years[18, 19], access to HMV and healthcare provision differs widely between countries, and HMV is underutilised in certain regions with standards differing across centres. Compared to the European HMV database[1], a similar amount of patients was invasively ventilated (12.4% vs 13%). The current data are therefore representative of large cohorts of patients on HMV which support the generalisability of our observations. However, in the alive group of patients treated with HMV for chronic respiratory failure in the large tertiary centre in which the study was conducted, the proportion of patients with OHS is higher and the proportion of patients with rapid progressive NMD smaller than in the study population of deceased patients. This support the conclusion of a favourable course on HMV in obesity-related respiratory failure and a short survival time in rapid progressive NMD on HMV. The proportion of patients on HMV with COPD and OHS differs between countries due to differences in interest in ventilation in COPD and in the prevalence of obesity. Overall, this large cohort of patients with chronic hypercapnic failure is representative of the major disease groups with an evidence-based indication for HMV.

So far, limited data have been available on the circumstances of death of patients on HMV. These data will help clinicians and the multidisciplinary team to inform patients on expected outcomes and might be considered in planning palliative community care and improve follow-up standards for patients with chronic respiratory organ failure. This also suggest that providing community services and building a network between home mechanical ventilation services and primary care is important for the successful care for these patients with a chronic disease. In addition, these data highlight the importance of regular follow-ups of patients of HMV to maintain or improve optimal HMV adherence and efficiency of ventilation since these factors are independent predictors of a favourable outcome. Further research in different disease groups with chronic respiratory failure to define optimal follow-up periods and examinations, ventilation settings and supportive care is needed to not only improve survival but also quality of life. In addition, more evidence on arguments for and against invasive HMV

is needed to guide clinical practice. The time-to-death on HMV in this cohort can be used for sample size estimation in future interventional trials on mortality in patients with an indication for HMV.

Limitations

Although this is the largest longitudinal analysis of patients with chronic hypercapnic respiratory failure deceased on HMV, an important limitation is that this is not a survival analysis. The database did not include all patients established on HMV, which is a cohort with continuous influx (patients newly initiated on HMV) and outgoing cases (death, change of caregiver, loss to follow-up) when studied longitudinally. In addition, the exact time on HMV in patients who died after being ventilated for longer than 10 years is not known (analysis time maximal 120 months). This analysis includes only patients who died on HMV and further information on censored patients (during or at the end of the study), which would be included in the probability estimates until their censoring, cannot be provided. Therefore, the absolute numbers of median-time-until-death might be underestimated and should be extrapolated to the whole cohort of patients on HMV with caution. A bias by late referral of patient groups not systematically screened for respiratory failure cannot be excluded. Another limitation is that no systematically collected data on the effect of HMV on symptomatic relief and quality of life can be provided at the present assessment, which is another important outcome besides survival; future databases collating these data from multi-centre collaborations would be helpful to describe minimal clinical important differences according to different cohorts.

Conclusion

The time-to-death while established on HMV differs significantly between disease groups with chronic hypercapnic respiratory failure. Patients with CWD, myopathy or OHS have a more favourable prognosis on HMV compared to patients with motor neurone disease, neuropathy, COPD or traumatic spinal cord injuries. Daily HMV treatment usage has a significant impact on the time-to-death. It is important to learn from mortality databases to plan end-of-life care for patients with chronic hypercapnic respiratory failure, as chronic hypercapnic respiratory failure remains a serious condition.

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Disclosure Statement

The authors have no conflicts of interest to declare.

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Author Contributions

Conception or design of the work: MM, EIS, JS. Acquisition of the data: all authors. Analysis: EIS. Interpretation of data: all authors. Drafting the work: EIS. Revising it critically for important intellectual content: all authors. Final approval of the version to be published: All authors. Agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved: JS.

Prof Joerg Steier is the guarantor for this work, had access to all data and controlled the decision to publish. He affirms that the manuscript is an honest, accurate, and transparent account of the study being reported and that no important aspects of the study have been omitted. The corresponding author attests that all listed authors meet authorship criteria and that no others meeting the criteria have been omitted.

Data sharing statement

No individual patient data will be shared.

FIGURE LEGENDS

Figure 1. Kaplan Meier curves for key groups and largest subgroups of neuromuscular disease. The Kaplan Meier curves over 10 years demonstrate the significant differences in the time on home mechanical ventilation until death between disease groups and between the largest subgroups of neuromuscular and chest wall disease (motor neurone disease and both myopathy and chest wall disease). CWD = chest wall disease. OVERLAP = Overlap Syndrome of COPD and obstructive sleep apnoea. MND = motor neurone disease. COPD = chronic obstructive pulmonary disease. OHS = obesity hypoventilation syndrome.

Figure 2. Whisker box plots (median, box: 25th to 75th percentiles, whiskers: adjacent values) comparing the time on HMV until death between different compliance groups. Compliance data were available in 1143 of 1210 patients who died on HMV. Of those, 265 used it <4h, 555 4-<12h, and 139 12-<24h (184 were 24h ventilator-dependent).

TABLES

Table 1

Characteristics	Total (n=1,210 [100%])	NMD & CWD (n=533 [44%])	COPD (n=296 [24%])	OHS (n=202 [17%])	OVERLAP (n=52 [4%])	OTHER (n=127 [11%])
Male, n (%)	671 (55)	314 (59)	150 (51)	99 (49)	32 (62)	76 (60)
Female, n (%)	539 (45)	219 (41)	146 (49)	103 (51)	20 (38)	51 (40)
Age [years (SD)]	65.1 (15.2)	62.6 (17.4)	69.2 (10.1)	66.5 (12.7)	70.6 (10.8)	61.7 (17.8)
Type of ventilation,						
NIV, n (%)	1,056 (87)	455 (85)	285 (96)	199 (99)	52 (100)	65 (51)
Tracheostomy, n (%)	150 (12)	74 (14)	11 (4)	3 (1)	0	62 (49)
NPV, n (%)	4 (<1)	4 (1)	0	0	0	0
Mode of ventilation						
PSV, n (%)	745 (62)	251 (47)	239 (81)	148 (73)	43 (83)	64 (50)
PCV, n (%)	408 (34)	248 (46)	53 (18)	44 (22)	6 (11)	57 (45)
AVAPS, n (%)	5 (<1)	1 (<1)	0	2 (1)	1 (2)	1 (1)
VCV, n (%)	1 (<1)	0	0	0	0	1 (1)
IPPV, n (%)	15 (1)	15 (3)	0	0	0	0
CPAP, n (%)	32 (3)	14 (3)	4 (1)	8 (4)	2 (4)	4 (3)
NPV, n (%)	4 (<1)	4 (1)	0	0	0	0
Ventilator settings						
Pressure support [cmH_2O]	15.4 (5.6)	14.5 (5.3)	18.3 (5.1)	14.5 (5.6)	13.8 (4.7)	14.4 (5.8)
IPAP [cmH_2O]	21.9 (7.6)	19.6 (8.5)	24.6 (6.9)	24.6 (5.1)	23.2 (4.9)	20.8 (5.7)
EPAP [cmH_2O]	6.6 (5.7)	5.3 (6.4)	6.3 (6.2)	10.0 (2.8)	9.5 (2.8)	6.1 (2.1)
Frequency [/min]	14.5 (4.5)	15.0 (4.6)	14.4 (5.8)	13.9 (2.9)	13.7 (3.2)	14.4 (2.5)
LTOT, n (%)	322 (27)	60 (11)	169 (57)	52 (26)	23 (44)	18 (14)
Compliance [hours/day]	9.6 (7.7)	11.3 (8.2)	7.0 (5.7)	6.0 (4.3)	5.8 (3.1)	16.0 (8.9)
Compliance Groups						
24h, n (%)						
12-24h, n (%)	184 (15)	104 (19)	14 (5)	4 (2)	0	62 (49)

4-12h, n (%)	139 (11)	99 (19)	22 (7)	9 (5)	1 (2)	8 (6)
0-4h, n (%)	555 (46)	207 (39)	153 (52)	121 (60)	37 (71)	37 (29)
Unknown, n (%)	265 (22)	103 (19)	78 (26)	59 (29)	13 (25)	12 (10)
	67 (6)	20 (4)	29 (10)	9 (4)	1 (2)	8 (6)

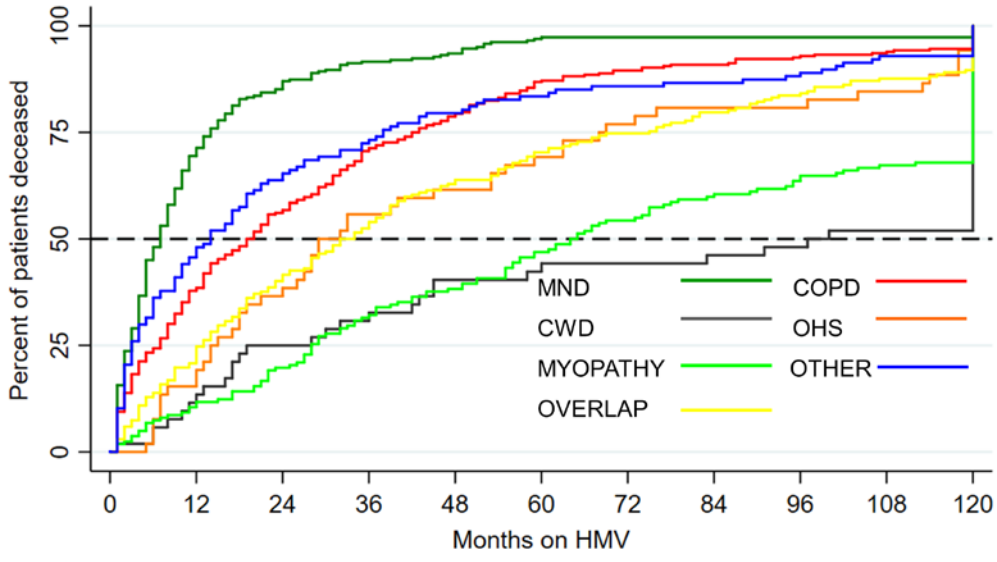
Table 1: Characteristics. Data are presented as mean (SD) unless otherwise stated (e.g. n (%). NMD and CWD = neuromuscular disease and chest wall disease. COPD = chronic obstructive pulmonary disease. OHS = Obesity related respiratory failure. OVERLAP = Overlap Syndrome between COPD and obstructive sleep apnoea. NIV = non-invasive ventilation. NPV = negative pressure ventilation. PSV = pressure-support ventilation. PCV = pressure-controlled ventilation. AVAPS = average volume-assured pressure support. VCV = volume-controlled ventilation. IPPV = intermittent positive pressure ventilation. CPAP = continuous positive airway pressure (included as used in hypercapnic OSA/OHS). LTOT = long-term oxygen therapy. IPAP = inspiratory positive airway pressure. EPAP = expiratory positive airway pressure.

Table 2

Group	Time-to-death, median (IQR; months)
All (n = 1,210)	**19.5 (6-55)**
NMD & CWD (n = 533)	**16 (5-59)**
Motor neurone disease (n = 262)	7 (3-14)
Myopathy (n = 162)	64.5 (28-120)#
CWD (n = 52)	98.5 (23.5-120)#
Neuropathy (n = 28)	10.5 (4-43.5)
Central (n = 9)	21 (2-58)
Unknown NMD (n = 20)	3 (1-22.5)
COPD (n = 296)	**19.5 (7-42.5)**
OHS (n = 202)	**33 (13-75)**
OVERLAP (n = 52)	**30.5 (14.5-68.5)**
OTHER (n = 127)	**14 (3-38)**
Traumatic (n = 37)	17 (3-39)
Hypercapnic central sleep apnoea (n = 9)	17 (3-96)
Interstitial lung disease (n = 6)	13 (6-50)
Unknown (n = 75)	12 (3-35)
NIV (n = 1,056)	20 (6-55)
Tracheostomy (n = 150)	17.5 (4-49)
NPV (n = 4)	>120

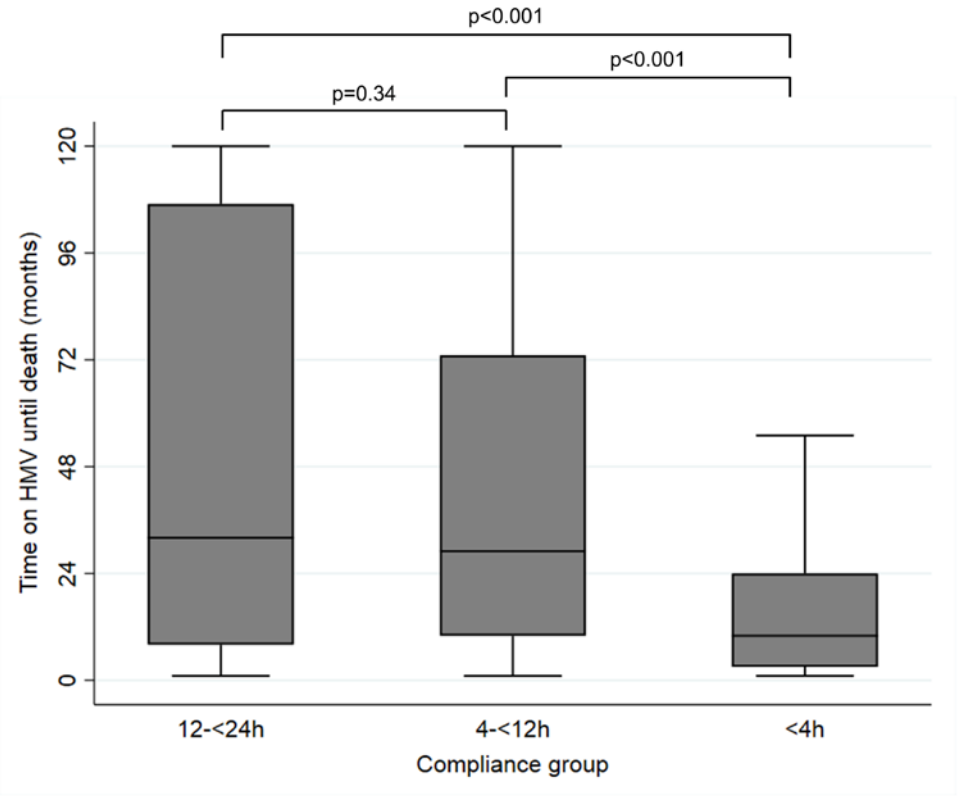
Median time-to-death. NMD and CWD = neuromuscular disease and chest wall disease. COPD = chronic obstructive pulmonary disease. OHS = OHS-related respiratory failure. OVERLAP = Overlap Syndrome between COPD and obstructive sleep apnoea. NIV = non-invasive ventilation. NPV = negative pressure ventilation. # The upper quartile may be higher (analysis period 10 years).

Figure 1



CWD	52	46	39	36	31	30	29	28	27	25	25
OVERLAP	52	44	33	23	20	16	12	10	10	8	3
MND	262	80	39	22	17	8	7	7	7	7	7
MYOPATHY	162	145	130	111	100	86	74	65	59	53	52
COPD	296	184	130	87	63	39	31	27	22	19	16
OHS	202	160	121	96	75	60	51	41	33	25	21
OTHER	127	69	46	35	26	21	18	17	15	9	9

Figure 2


p<0.001
p<0.001
p=0.34
Time on HMV until death (months)
0
24
48
72
96
120
12-<24h
4-<12h
<4h
Compliance group

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