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"A randomized trial of initiation of chronic non-invasive mechanical ventilation at home vs in-hospital in patients with Neuromuscular Disease and thoracic cage disorder"

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“A randomized trial of initiation of chronic non-invasive mechanical ventilation at home vs in-hospital in patients with Neuromuscular Disease and thoracic cage disorder”: The Dutch Homerun Trial

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Competing interests

Dr. van den Biggelaar reports personal fees from Philips, and Westfalen Medical B.V., both outside the submitted work. Dr. Hazenberg, Dr. Cobben, Dr. Gaytant and Dr. Vermeulen have nothing to disclose. Prof. Dr. Wijkstra reports grants from ZONMW, grants from VIVISOL, during the conduct of the study; grants and personal fees from Philips, grants and personal fees from RESMED, grants from Goedegebuure, grants from vital air, personal fees from Bresotec, and personal fees from Synapse, outside the submitted work.

Prior abstract publication/presentation

The results of this study have been presented at the European Respiratory Society congress 2019 in Madrid.

1 **Abbreviations list**

ALS	Amyotrophic Lateral Sclerosis
BMI	Body Mass Index
CBS	Centraal bureau voor statistiek; Statistics Netherlands
CI	confidence interval
COPD	Chronic obstructive pulmonary disease
CPAP	continuous positive airway pressure
EPAP	expiratory positive airway pressure
EQ-5D	EuroQol-5Dimensions questionnaire
FSHD	Facioscapulohumeral dystrophy
FVC	Forced Vital Capacity
HADS	Hospital Anxiety and Depression Scale
HCO ₃	Bicarbonate
HMSN	Hereditary Motor and Sensory Neuropathy
HMV	Home Mechanical Ventilation
HRQoL	Health-Related Quality of life
IBM	International Business Machines
ICU	intensive care unit
IPAP	inspiratory positive airway pressure
MCU	medium care unit
MD	Myotonic Dystrophy
MIP	Maximal inspiratory pressure
MRF-28	Maugeri Respiratory Failure
MS	Multiple Sclerosis
NIV	Non-invasive Ventilation
NMD	neuromuscular disease
OHS	Obesity Hypoventilation Syndrome
PaCO ₂	partial arterial carbon dioxide pressure
PaO ₂	partial arterial oxygen pressure
PEEP	positive end-expiratory pressure
PSMA	Progressive Spinal Muscular Atrophy
PtcCO ₂	transcutaneous measured CO ₂ pressure
QALY	Quality-adjusted life year
RCU	respiratory care unit
SaO ₂	oxygen saturation
SD	standard deviation
SF-36	Short-Form Health Survey
SMA	Spinal Muscular Atrophy

Abstract:**Background**

There is an increasing demand for Home Mechanical Ventilation (HMV) in patients with chronic respiratory insufficiency. At present, Non-invasive Ventilation (NIV) is exclusively initiated in a clinical setting at all 4 centres for HMV in The Netherlands. In addition to its high societal costs and patient discomfort, commencing HMV is often delayed due to lack of hospital bed capacity.

Research Question

Is HMV initiation at home, by using telemonitoring, non-inferior to in-hospital initiation in a nationwide study?

Study design and Methods

We conducted a nationwide, randomised controlled non-inferiority trial, in which every HMV centre recruited 24 patients (home (n=12) vs hospital (n=12)) with a neuromuscular disease (NMD) or thoracic cage disorder, all with an indication to start HMV. Change of arterial carbon dioxide (PaCO_2) over a 6-months period was considered the primary outcome, while quality of life and costs were assessed as secondary outcomes.

Results

A total of 96 patients were randomised, most of them diagnosed with NMD. We found a significant improvement of the PaCO_2 within both groups (home from 6.1 kPa to 5.6 kPa ($p < 0.01$), hospital from 6.3 kPa to 5.6 kPa ($p < 0.01$)), with no significant differences between groups. Health-Related Quality of life (HRQoL) showed significant improvement on various subscales; however, no significant differences were observed between the home and hospital groups. From a societal perspective, a cost reduction of over €3200- per patient was evident in the home group.

Interpretation

This nationwide, multi-centre study shows that HMV initiation at home is non-inferior to hospital initiation, as it shows the same improvement in gas exchange and HRQoL. In fact, from a patient's perspective, it might even be a more attractive approach. In addition

Keywords: non-invasive ventilation; neuromuscular disease; thoracic cage abnormality; telemedicine

Patients with chronic respiratory failure due to thorax cage disorder or neuromuscular diseases are suitable candidates for home mechanical ventilation (HMV)¹⁻³. In the Netherlands, HMV usually starts in the hospital on a respiratory ward or intensive care unit, as recommended in the Dutch National guideline⁴. Unfortunately, this is a costly treatment requiring hospital bed occupation. Over the last decade, the 4 Dutch centres for HMV faced an annual ~10% growth in patient number, exceeding the bed capacity of the departments and leading to an increase of patients on the waiting list.

Patients usually prefer to stay in their home environment to optimally benefit from tailor-made health care provision, exactly fulfilling their needs. In addition, it is almost impossible to obtain the same level of care in the hospital. Therefore, initiation of HMV at home would make sense, both from a patient perspective and in terms of healthcare funds and hospital capacity.⁵

One of the 4 Dutch centres for HMV conducted a local randomised non-inferiority trial comparing initiation of HMV at home versus the hospital⁶. This study showed comparable results for gas exchange and quality of life between the two groups and indicated that home initiation is safe, technically feasible, and cheaper compared to the in-hospital initiation. More recently, home initiation of non-invasive ventilation (NIV) was shown to be non-inferior to in-hospital initiation in severe COPD patients⁷.

Although there is a high level of collaboration and cooperation between the 4 Dutch centres, which combined manage all HMV patients in the Netherlands, marked differences are evident in their organisations. Therefore, a national multicentre study (including all 4 centres) is necessary to properly evaluate initiation of HMV at home and, based on the results, potentially introduce it as the standard care in the Netherlands.

By using a telemonitoring approach, we hypothesise that initiation of HMV at home,

as the primary outcome, while quality of life and societal costs were assessed as secondary outcomes.

Methods

Patients from all 4 Dutch centres for HMV were recruited for this prospective randomised controlled non-inferiority trial. Every centre included 24 patients and obtained written informed consent. The UMCG institutional review board, approved this study (approval number 2014/529), Monitoring was performed on all sites by an external monitor, and a Data Safety Monitoring Board was installed. The study was registered in the Dutch trial register (NTR4683) and later internationally (Clinicaltrials.Gov ID: NCT03203577).

Inclusion and exclusion criteria

Patients had to meet all of the following inclusion criteria: diagnosis of NMD or thoracic cage disorder with the indication for HMV based on presence of symptoms of alveolar hypoventilation (fatigue, headache of dyspnoea) combined with all the following elements: 1) arterial carbon dioxide > 6.0 kPa daytime **or** arterial or transcutaneous carbon dioxide > 6.0 kPa at night for a period of time **or** orthopnoea as a result of diaphragm paralysis^{4,8}; 2) over 18 years of age; 3) the existence of a sufficient network (social or professional) according to the supervising center for HMV (allowing for safe HMV initiation at home). Patients who had previously received non-invasive ventilatory support of any form or CPAP therapy were excluded. In addition, subjects requiring invasive ventilatory support or those residing in nursing homes were also excluded.

Randomisation and intervention

We used ALEA randomisation software (Forms Vision BV) with stratification for Amyotrophic Lateral Sclerosis (ALS) to obtain balance for this diagnosis in both groups. The control group consisted of patients that started HMV in the hospital as standard care, while the

Measurements

The change in daytime PaCO₂ after 6 months compared to baseline was assessed as the primary outcome. Blood samples for determining PaCO₂ were obtained from the a. radialis. Quality of life was evaluated at baseline and after 2 and 6 months by using different questionnaires: Severe Respiratory Insufficiency (SRI)⁹, Maugeri Respiratory Failure (MRF-28)¹⁰, Short-Form Health Survey (SF-36)¹¹, and the Hospital Anxiety and Depression Scale (HADS)¹². We compared the absolute costs and costs in relation to QALY's using The EuroQol-5Dimensions questionnaire (EQ-5D¹³) and Dutch reference prices for health care consumption, travel- and productivity costs¹⁴.

Initiation of home mechanical ventilation

Standard operating procedures were implemented to obtain equal initiation in each centre. We aimed to use the ResMed ASTRAL 100/150 (ResMed, San Diego, United States of America) for non-invasive ventilation in both groups. Transcutaneous assessment of gas exchange for the home group was performed with the Sentec device (Sentec AG, Therwil (Basel)Switzerland). Data from the Astral non-invasive ventilator was transmitted via the Carecomm and the SENTEC via Dynavision (both from Techmedic BV). Unfortunately, due to connectivity problems, we were forced to start the study with the ResMed Elisée in combination with the Dynavision, and link the Sentec to a separate Dynavision. As soon as the technical issues were resolved, the Astral 100/150, instead of the Elisée, was used and connected to the CareComm unit (Techmedic BV), as per the original design.

Standard procedure (all patients):

The interface was considered in the following order: an initial nasal mask followed by full-face-, mouth- or total-face mask, depending on the best individual fit. The ventilator was set up in the S/T mode with an inspiratory pressure of 10 cmH₂O, a positive end-expiratory pressure (PEEP) of 4 cmH₂O, a target volume of 8-10 ml/kg, and a ventilatory rate close to the patients breathing frequency. The standard procedure also described which actions should be taken to adjust the ventilator to achieve normocapnia during the night.

care unit (MCU) or respiratory ward, and in Rotterdam strictly at the intensive care unit (ICU). In each of these centres, the trained staff manages the patients, adjusting the ventilator to the patient's needs, and educating patients and family, all in exactly the same way. Patients were discharged when optimal gas exchange and comfort was achieved. Follow-up occurred two and six months after initiation. At six months, follow-up at the outpatient clinic included assessment of arterial blood gas and lung function, if feasible, and questionnaires were filled out.

Initiation at home

The ventilator, humidifier, Sentec, and corresponding telemonitoring devices were installed in the patient's bedroom. During the first visit, patients and caregivers were instructed by the specialised nurse followed by one or more practice sessions on about the procedures and how to use the ventilator and mask. The training was specifically tailored to the needs of the individual patients and their caregivers. The first use of the ventilator was done under supervision of the specialised nurse for titrating the therapy as described in the standard *procedure*. The patient and the specialised nurse made a practice scheme and agreed when the daily evaluation was done. Follow-ups and meetings other than those at 2 and 6 months were not described in the protocol, as they were arranged only upon request by the patient, caregiver, or nurse. If there were any questions or problems, a 24/7 service was available. Follow-up took place after two and six months, the last in the outpatient clinic, after starting HMV, in a similar fashion, also including arterial blood gas, as described for hospital initiation.

Telemonitoring:

During the initiation period, ventilator data and transcutaneous CO₂ measurements were collected. Data were encrypted and sent anonymously; the decrypting key was installed on the laptop of the nurse. Results were usually evaluated over the phone, but when necessary a home visit took place. The nurses interpreted the data and decided if additional follow-up was needed.

For adequate comparison between the 2 groups, all cost items were registered, including days of admission, time spent on the phone (by nurses), travelling distance, and time spent on home visits. Furthermore, information on visits by other health care workers, such as physiotherapists and general practitioners, was gathered during the 6 months of follow-up. Volumes of healthcare consumption were multiplied with the available reference price¹⁴ (€), as indexed to the price level of 2018 (CBS). Absenteeism costs were calculated by multiplying the number of missed work hours with the average hourly productivity costs of paid work in the Netherlands¹⁵ (online e-table 1). Total costs were computed on a patient level, and means were presented separately for the two groups. Finally, bootstrap analyses were performed (5000 replications of the dataset) to generate alternative 95% confidence intervals surrounding the point estimates.

Statistics

The electronic database was generated by OpenClinica (Version: 3.12.2 OpenClinica, LLC Waltham, USA) and analysed in SPSS vs 24 (IBM). We defined a non-inferiority margin of less than 0.5 kPa for the difference in change of the CO₂. This was based on the study of Hazenberg who used 0.5 kPa as a non-inferiority margin and did not find significant differences in change for quality of life between both arms.⁶ For proper statistical evaluation, with an alpha of 0.05, a beta of 0.2, and a standard deviation of 0.71, two groups of 36 patients are necessary. Based on dropout rates from our previous pilot study a total of 96 patients was required. Analyses were performed using data from all patients with available baseline and 6-month measurements.

The null hypothesis was tested by calculating the change in PaCO₂ from baseline to 6 months by applying linear regression methods with correction for the baseline value. The adjusted mean difference between groups was calculated. This method was used for all other outcomes if the residual of the regression model was normally distributed.

Results

219, Utrecht 232, Maastricht 428 and Rotterdam 593 days; all patients committed between July 2015 and August 2017. The 6 main reasons for exclusion were: 114 patients had a diagnosis different than NMD or thoracic cage disorder, 53 patients were under 18 years of age, in 39 cases the network was not sufficient to start at home, 77 subjects required acute or semi-acute NIV, 54 patients had used NIV before, and 85 patients initiated HMV in another hospital for logistic reasons. Reason for exclusion for the other 90 patients is provided online in e-table 2.

A total of 96 patients were randomised: 49 patients in the hospital and 47 in the home group. A great variety of diagnoses were included, with ALS dominantly represented (Table 1). At baseline, both groups were comparable except for a small difference in PaO_2 (Table 2). From the home group, 1 patient was withdrawn after admitting to previous CPAP use. Waiting time for NIV initiation at the hospital was 31.2 versus 19.9 days at home. The average number of days spent on the initiation process in the hospital was 4.9 and 15.9 at home. Time spent at an ICU, MCU, RCU, or general ward averaged 2.5, 3.3, 4 and 6.4 days, respectively. A total of 23 patients were lost during follow-up: 16 people died; 2 of them before initiation took place, and 10 subjects used palliative sedation or underwent euthanasia because of progression of their underlying disease (mainly patients suffering from ALS). Another 7 patients were lost for follow-up due to several other reasons, including lack of mobility to visit the hospital. In total, 73 patients, 36 in the home and 37 in the hospital group, reached the endpoint after 6 months of follow-up.

Gas- exchange

The primary outcome, daytime PaCO_2 , improved significantly after initiation of treatment in both groups, as evident from the results after 6 months of follow-up (Table 3). The adjusted mean difference between groups was 0.01 kPa, which was not significant; hence, based on the PaCO_2 , initiation at home was non-inferior to initiation at the hospital (Figure 2). Similar results were observed for the nocturnal transcutaneous CO_2 exchange (Table 4). Lastly, PaO_2 and HCO_3 levels improved significantly over a 6-month treatment period as well, without

Quality of life questionnaires

Patients from both groups had some significant improvements in the (sub)scores of the different questionnaires between baseline and 6 months. However, there were no significant differences found between the home and hospital group. (See e-table 3)

Therapy compliance and settings:

The compliance during the night after 6 months amounted to 6.9 ± 2.7 and 6.9 ± 3.3 hours for the hospital and home group, respectively, which was not significantly different between groups. Most patients used the ventilator only during the night, less than 10% used it during daytime on demand. There were 41 patients using the ResMed Elisée and 52 the ResMed Astral. The settings after 6 months for the hospital group were: IPAP 16.8 ± 4.6 cmH₂O, EPAP 5.8 ± 1.8 cmH₂O, and back-up frequency 14.7 ± 2.8 ; and for the home group: IPAP 16.0 ± 3.7 cmH₂O, EPAP 5.4 ± 1.7 cmH₂O, and back-up $14.1 \pm \text{SD } 2.6/\text{min}$.

Costs analysis

Cost analysis from a social perspective showed an average saving of €3225 (95% CI: 4279 to 2107) per patient when ventilatory support was started at home rather than at the hospital (Table 5). As indicated, during this 6-month study period no significant differences in QALYs (0.25 vs. 0.26) were observed between both groups; thus, initiation at home resulted in lower costs, while patients experienced the same quality of life as NIV patients in the hospital. The main difference in costs was explained by the reduced number of admission days. Costs for care provided by nurses, including travel expenses, and costs for services by a General Practitioner and/or other caregivers, were higher in the home group, while income lost due to absenteeism was lower in the home group.

Time spend by nurses.

The mean total time spent by the nurses was 19.1 hours in the home group versus 12.6 hours in the hospital group; the mean number of contact moments was 13.6 and 12.3 in the

Discussion

This national study, including all 4 Dutch centres for HMV, shows that initiation of NIV at home is not inferior to initiation at the hospital with respect to gas exchange, safety and quality of life, and reduces costs in the patient population included. Based on the results of this unique study, we will now recommend to update the national guideline with a statement that initiation of NIV can take place at home, with similar, satisfactorily, predicted clinical and improved financial outcomes as in a hospital setting for the patient population studied. There is only one other study that evaluated initiation of NIV at home in a similar group of patients; however, this was in a monocentre setting, with mostly similar results, with the exception of a higher baseline PaCO₂ (6.6 kPa) than in our study probably due to the large group of ALS patients we included⁶. In addition, Duiverman recently published findings using the same set up in severe COPD patients⁷. Both these studies show a significant decrease in PaCO₂ in the home group and non-inferiority to hospital initiation, with roughly the same amount of cost reduction^{6,7}.

In one of the first randomised controlled studies on HMV initiation outside the hospital, HMV was compared during inpatient and outpatient initiation¹⁶; however, the patient population was very different from ours, as ALS patients were excluded and children were included. Also, inpatient initiation ended when a patient was able to use the device, could handle the mask and was able to sleep with the device for a couple of hours. In contrast, initiation of the outpatient group consisted of one mandatory visit and, if needed, 2 more visits at the outpatient clinic (one-week interval). Follow-up with patients took place by planned telephone calls. During the home visits, with a duration of 30 to 45 min each, the ventilator settings could be adjusted, with control of oxygen saturation. However, in contrast to our study, CO₂ levels were not measured and telemonitoring was not performed during initiation. In the same study, both groups had a follow-up after 2 months, which included overnight hospitalisation for optimisation of the ventilator settings. The results between the groups were comparable for most parameters; however, there was a significant difference in CO₂ reduction after 5 months favouring the outpatient group¹⁶.

1 difference in the effectiveness of ventilation was seen between both groups. Reduced
2 waiting time and improved survival were observed following the introduction of the
3 outpatient model compared to the inpatient initiation. Of note, the patients involved in this
4 study strictly suffered from motor neuron disease, unlike the participants in our study.

5 A more recent study showed that outpatient initiation of NIV in patients with ALS is not
6 inferior to inpatient initiation in terms of patients' acceptance and adherence to NIV¹⁸. Lung
7 function tests, like MIP and FVC <70% predicted, were used as inclusion criteria, whereas
8 complaints of respiratory failure and/or hypercapnia were not considered an indication for
9 HMV (in contrast to our study). Results revealed that early outpatient initiation is as effective
10 as inpatient initiation. However, due to completely different inclusion criteria, it is difficult
11 (and inappropriate) to directly compare their results with ours.

12 Despite the positive results, our current study has a few limitations. As a large number of ALS
13 patients was included, NIV was started because of orthopnoea without daytime hypercapnia
14 in several of these patients, resulting in a very modest baseline CO₂ elevation during
15 daytime. On the other hand, nocturnal transcutaneous assessment showed that patients
16 were hypoventilating, which is an indication for HMV. In addition, in a landmark study on
17 NIV in ALS patients, 38 out of 41 patients were included based on orthopnoea, and only 18
18 were hypercapnic¹⁹. This suggests that orthopnoea without hypercapnia is an accepted
19 indication for starting NIV in ALS patients. Especially in ALS patients, the home initiation of
20 NIV is a huge advantage as they can stay at home in their familiar environment with involved
21 caregivers, who know exactly the specific needs of these severely disabled patients. Another
22 weakness is that different groups of patients have been included. However, our study
23 contained only 11 patients with a thoracic cage problem and 85 with an NMD which shows
24 that the focus was primarily on NMD.

25 Introducing new technologies into the health care system is challenging, both in terms of
26 privacy and lack of standardisation in IT-communication protocols. Initially, we were
27 challenged by connectivity issues regarding sending and/or receiving data, most often due to
28 inferior connection units or weak network signals at the patient's home. Consequently, the

Despite the longer initiation time at home than at the hospital, with equal effectiveness after 6 months, at home patients can spend time on their own terms until HMV is comfortable rather than 'being stuck' in a hospital regime.

Regarding societal costs, there appeared to be a little more time spent by the nurses with patients in the home group, which was anticipated due to home visits; however, we cannot explain the increase in costs related to care by general practitioners and other miscellaneous caregivers.

In terms of costs and translating some of our findings to other international institutions, it is difficult to compare standard hospital initiation in The Netherlands to specific situations in other countries, where initiation often takes place in outpatient clinics. In addition, the Dutch organisation is very specified as specialised nurses supervise the patients during their start in hospital and do the follow up at home as well. To further improve this unique system, we believe that the patient would benefit the most if they start at home and not at the outpatient clinic.

Also, in The Netherlands, specific education for caregivers is accommodated by a national HMV educational program; this blended learning program contains online courses combined with practical training for caregivers and even with examination for care professionals. Implementing such a program in individual, international centres could represent an expensive investment.

Interpretation

This study showed that initiation of NIV at home in patients with chronic hypercapnic respiratory insufficiency due to NMD or thoracic cage disorder is not inferior to initiation at the hospital. In addition to an equally improved gas exchange and quality of life, we found an average cost reduction of €3225.- for patients that initiated HMV at home. We will recommend, in our national guideline, to start HMV at home.

Take Home Points

- This nationwide, multi-centre study shows that HMV initiation at home is non-inferior to hospital initiation, as it shows the same improvement in gas exchange and HRQoL. In addition starting at home saves over €3200,- per patient over a 6-month period.
- We will recommend, in our national guideline, to start HMV at home.

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Author contributions: P.W. is the guarantor of the manuscript. R.B. and P.W. were the primary authors of the paper. A.H., N.C. and M.G. assisted with data collection, which was confirmed by R.B. The statistical analysis was provided by R.B. A.H. K.V. and P.J., All authors were involved in interpretation of data and contributed to critical revision of important intellectual content and final approval of the version to be published.

Competing interests

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1 **Table 1** Diagnosis of all included patients

Diagnosis	Home (n)	Hospital (n)
Amyotrophic Lateral Sclerosis (ALS)	22	20
Diaphragm paralysis	6	9
Myotonic Dystrophy (MD)	8	4
Progressive Spinal Muscular Atrophy (PSMA)	2	3
Obesity Hypoventilation Syndrome (OHS)	2	3
Restriction/scoliosis	2	4
Facioscapulohumeral dystrophy (FSHD)	2	0
Hereditary Motor and Sensory Neuropathy (HMSN)	1	0
Multiple Synostosis Syndrome	1	0
Multiple Sclerosis (MS)	0	2
Becker muscular dystrophy	0	1
Spinal Muscular Atrophy (SMA)	0	1
Post-polio syndrome	0	1
Myofibrillar myopathies	0	1
Total number of patients	46	49

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	Home (N= 46)	Hospital (N= 49)	P-value
Male, n	32	34	0.99
Age in years, mean (SD)	55.7 (14)	58.2 (12)	0.36
BMI kg-m2, mean (SD)	26.1 (5.4)	27.4 (6.6)	0.29
pH, Mean (SD)	7.42 (0.03)	7.41 (0.03)	0.11
PaCO ₂ kPa, mean (SD)	6.0 (0.9)	6.2 (0.9)	0.29
PaO ₂ kPa, mean (SD)	10.9 (2.6)	9.8 (1.2)	0.01
SaO ₂ %, mean (SD)	95.0 (3.3)	93.7 (3.1)	0.05
HCO ₃ mmol/l, mean (SD)	28.6 (3.50)	28.7 (3.8)	0.93
VC % predicted, mean (SD)	63.3 (18.6)	58.9 (19.4)	0.27
Sub-category ALS patients			
Diagnosis ALS	22	20	0.49
Male, n	18	14	0.37
Non-Bulbar, n	11	12	0.52
Time from ALS diagnosis to study inclusion [months]	15.6 (13)	16.6 (17)	0.82
Age [years] on time of diagnosis	57.9 (12)	60.9 (11)	0.40

Table 2 Baseline characteristics.

Data are shown as mean and standard deviation (SD) unless indicated otherwise. BMI: Body Mass Index; pH: potential of Hydrogen; PaCO₂: partial arterial carbon dioxide pressure; PaO₂: partial arterial oxygen pressure; SaO₂: oxygen saturation; HCO₃: bicarbonate; VC % predicted: % of the predicted vital capacity. Sub-category ALS patient; separate expression for ALS patient because of the dominance of this diagnose.

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	Home N=37			Hospital N=36			Adjusted mean difference in change home vs. in-hospital (95% CI)
	Baseline	6 months	p-value	Baseline	6 months	p-value	
PaCO₂, kPa	6.0 ± 0.8	5.6 ± 0.7	<0.01	6.3 ± 1.0	5.6 ± 0.9	<0.01	0.01 kPa (-0.36 to 0.38)
PaO₂, kPa	10.4 ± 2.1	11.0 ± 2.8	0.12	9.5 ± 1.8	10.9 ± 2.3	<0.01	-0.58 kPa (-1.62 to 0.46)
HCO₃, mmol/l	28.9 ± 3.2	26.9 ± 2.4	<0.01	28.9 ± 4.0	26.5 ± 3.3	<0.01	0.36 mmol/l (-1.5 to 1.2)

2 **Table 3 Daytime arterial blood gasses**

3 Data are shown as mean and standard deviation ± SD. PaCO₂: partial arterial carbon dioxide pressure;
4 PaO₂: partial arterial oxygen pressure; HCO₃: bicarbonate. A positive mean difference indicates a
5 reduced decrease (PaCO₂, HCO₃), or an increase (PaO₂) for the home compared to the hospital
6 group.

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Table 4 Nocturnal transcutaneous gas exchange

	Home			Hospital			Adjusted mean difference in change home vs. in-hospital (95% CI)
	Baseline	6 months	p-value	Baseline	6 months	p-value	
PtcCO₂ (kPa)	6.4 ± 1.1	5.5 ± 0.9	<0.01	7.0 ± 1.2	5.6 ± 0.9	<0.01	-0.07 (-0.71 to 0.57)
Maximal PtcCO₂ (kPa)	7.5 ± 1.4	6.3 ± 1.0	<0.01	8.1 ± 1.5	6.6 ± 1.8	<0.01	-0.05 (-0.68 to 0.59)
SpO₂ (%)	92.4 ± 5.1	94.8 ± 3.0	0.03	91.1 ± 3.2	94.2 ± 2.1	<0.01	0.69 (-1.15 to 2.54)

Data are shown as mean and standard deviation ± SD. PtcCO₂, transcutaneous measured CO₂ pressure, the mean and maximum were recorded. SaO₂: oxygen saturation. A positive mean difference indicates a reduced decrease (PtcCO₂, mean and max), or an increase (SpO₂) for the home compared to the hospital group.

Table 5 Comparison of costs and cost-effectiveness between the home and hospital group

	Home	Hospital
	Mean (ds)/Mean (95% CI bootstrap)	Mean (ds)/Mean (95% CI bootstrap)
QALY 6 months	0.26 (0.16)	0.25 (0.15)
<i>Direct medical costs</i>		
Hospital admission	€0 (0-0)	€3046 (2528-3421)
Costs nurses	€781 (663-921)	€496 (404-578)
General practitioner	€161 (107-218)	€95 (67-120)
Medical specialist	€296 (162-542)	€355 (252-456)
Miscellaneous caregivers	€77 (32-132)	€28(6-56)
<i>Indirect non-medical costs</i>		
Absenteeism	€185 (0-524)	€708 (11-1939)
Total (social perspective)	€1500 (1166-1970)	€4725 (3716-5731)

(PM max is 0.5 due to the fact that the study period was only 6 months)

Figure legends**Figure 1 Consort Diagram of the Homerun study**

Flow diagram of included patients (CPAP, continuous positive airway pressure).

Figure 2. Non-inferiority analysis for PaCO₂.**Figure 3 Total and subcategorized time spent by nurses during the initiation and 6-month follow-up period.**

Time spent during initiation and 6 months of follow-up by the nurses in mean 1) phone calls: time spent by the respiratory nurse on the phone with the patients; 2) travelling: nurse's travel time to the patients; 3) home visit: time spent by the nurse with the patient during a home visit; 4) clinic: time spent by the nurse with the patient during hospitalization.