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"HOSPITAL AT HOME" FOR NEURO-MUSCULAR DISEASE PATIENTS WITH RESPIRATORY TRACT INFECTION: A PILOT STUDY.

Andrea VIANELLO, MD[1]; Francesca SAVOIA, MD[1]; Emanuela PIPITONE, PhD[2]; Beatrice NORDIO, MD[3]; Giulia GALLINA, RRT[4]; Luciana PALADINI, MD[1]; Alessandra CONCAS, MD[1]; Giovanna ARCARO, MD[1]; Federico GALLAN, MD[1] and Elena PEGORARO, MD[5]

[1] Respiratory Pathophysiology and Intensive Care Unit, City Hospital of Padova, Padova, Italy

[2] Department of Formative Sciences, University of Modena and Reggio Emilia, Modena, Italy

[3] Respiratory Home Care Service, Padova, Italy

[4] UILDM Rehabilitation Centre, Padova, Italy

[5] Department of Neurosciences, University of Padova, Padova, Italy

This work was performed at University-City Hospital, Padova, Italy

Correspondence: Andrea Vianello, MD
U.O. Fisiopatologia Respiratoria
Azienda Ospedaliera di Padova
Via Giustiniani, 2
35128 PADOVA – Italy
Phone: 0039-049-8218587
Fax: 0039-049-8218590
avianello@qubisoft.it

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STATEMENT OF INTERESTS

We all Authors declare that we have no financial and personal relationships with people or organizations that could have inappropriately influenced (bias) our work. No study sponsor has been involved in the study design, in the collection, analysis and interpretation of data; in the writing of the manuscript; and in the decision to submit the manuscript for publication. We have no conflicts of interest to declare.

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ABSTRACT

Background: The “Hospital at home” (HH) model may provide adequate care without an adverse effect on clinical outcome and is generally well-received by users. Our objective was to compare HH and inpatient hospital care for Neuro-Muscular Disease (NMD) patients with Respiratory Tract Infection (RTI).

Methods: *Design*: Prospective randomised controlled trial. *Setting*: University teaching hospital offering secondary care service to 500,000 patients. *Patients*: Selected NMD patients with RTI where hospital admission had been recommended after medical assessment. *Interventions*: HH was provided as an alternative to inpatient admission. *Main outcome measures*: need for hospitalization, treatment failure, time to recovery, death during the first 3 months following exacerbation, cost of patient care.

Results: Among 59 consecutive NMD patients eligible for the study, 53 met the criteria for HH. Twenty-six patients were randomised to home care and 27 to hospital care. No significant differences were found in treatment failure (8/26 vs 13/27, p=0.19), time to recovery (8.9 ± 4.6 vs 9 ± 8.9 days p=0.21) or mortality at three months (3/26 vs 4/27 deaths; p=0.42) between the groups. HH failure was independently correlated with type of NMD (p=0.0037) with an OR of failure of 17.3 (95% CI, 2.1 to infinity) for patients with Amyotrophic Lateral Sclerosis. The total and daily direct cost of patient healthcare was significantly lower for the patients who were successfully treated at home compared to hospitalised individuals.

Conclusions: HH is an effective alternative to hospital admission for selected MND patients with RTI.

KEYWORDS: Neuromuscular Disorder; Acute Respiratory Failure; Non-Invasive Ventilation; Hospital at Home; Amyotrophic Lateral Sclerosis; Respiratory Tract Infection

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INTRODUCTION

Hospital at home (HH) is defined as “a service that provides active treatment by health care professionals, in the patient's home, of a condition that otherwise would require acute hospital in-patient care, always for a limited period” (1).

In recent years HH services have reached widespread diffusion for patients with a variety of conditions including exacerbation of chronic obstructive pulmonary disease (COPD), diabetes (uncontrolled or ketoacidosis), congestive heart failure and recovery from stroke or from surgery for hernia or hip replacement (1,2).

The development of the HH model is based on the overwhelming finding that this scheme may provide adequate care without an adverse effect on clinical outcome and the fact that it is generally better received by users, since patients managed at home express greater satisfaction with care than those in hospital (2,3); in addition, although the economic effects of home care programs are still controversial, studies have reported that hospital in the home can be associated with substantial cost savings (4,5).

Respiratory Tract Infections (RTIs) represent the most common cause of hospitalisation for Neuro-Muscular Disease (NMD) patients, punctuating the clinical course of these individuals and triggering over 90% of episodes of Acute Respiratory Failure (ARF) (6). ARF may be caused by airway mucous accumulation, atelectasis and ultimately blood gas derangement, and can require intensive respiratory assistance and close monitoring (7).

Uncontrolled clinical trials have shown that RTIs in NMD patients can be effectively managed by a home care protocol based on the combination of continuous Non-Invasive Ventilation (NIV), intensive Manually and/or Mechanically Assisted Coughing (AC) and arterial oxygen saturation (SaO_2) monitoring, preventing or reversing oxyhemoglobin desaturation and reducing the need for hospitalizations, intubation, and tracheotomy (8,9).

Based on these encouraging results and the observation that avoidance of hospital admission is a highly valued outcome for NMD individuals, maintaining the independence

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of the patient and his/her family and increasing their Quality of Life (QoL) (10), we were prompted to evaluate the efficacy and safety of a HH model for the management of RTIs in NMD patients. To this end, we analysed the clinical course of 26 subjects with advanced NMD who developed severe RTI requiring hospital admission and were treated at home and compared the results with the outcomes of 27 patients who received conventional hospital care. In particular we hypothesised that HH for selected NMD patients might have an impact on clinical outcome similar to standard inpatient hospitalisation, and that the application of the HH model might reduce the direct costs of patient care.

METHODS

This study was approved by the Institutional Review Board of our Ethics Committee.

We evaluated the clinical course of 26 NMD patients suffering from severe RTI who were treated by a HH program (study group) and compared their outcomes with the outcomes of a population of 27 control patients who were hospitalised (control group). The patients were provided with written information about the study and gave their informed consent to be assisted by the HH program; those younger than 18 years of age reached this decision in accordance with their parents.

Patients

We conducted the study at the Respiratory Pathophysiology Division of the City Hospital of Padova. All consecutive NMD patients who were referred to the emergency department of our Hospital or to the outpatient clinic of our Division between January 2009 and December 2011 with RTI and urgent need for hospitalisation were recruited.

The diagnoses of NMD were based on standard clinical, enzymatic, electromyographic, DNA, and biopsy data. The diagnosis of RTI was based on the presence of one or more of the following symptoms or signs: fever, throat irritation or sore throat, hoarseness, and cough. The accumulation of airway mucous was defined as the coexistence of

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auscultatory ronchi and oxyhemoglobin desaturation (SaO_2< 95%) (8,11). The diagnosis of pneumonia was based on the concomitant presence of infiltrates on chest x-ray. Urgent need for hospitalisation was defined as the occurrence of one of the following: (a) difficulty in breathing; (b) need for continuous non-invasive ventilatory support; (c) oxyhemoglobin desaturation with need for assisted coughing (8).

Patients showing one of the following exclusion criteria were considered ineligible for the study: 1) requirement for critical care with 24-hour surveillance; 2) living outside the geographic area followed by our district nurse service; 3) lack of non-professional caregivers or caregiver networks at home; and 4) presence of an advance directive declining to undergo intubation and/or cardiopulmonary resuscitation (CPR).

Recruited patients were randomised in a ratio of 1:1 for the HH program (study group) or hospital admission (control group), using blinded sealed envelopes.

Measurements

Baseline characteristics of the 2 groups are compared in Table 1. The following data were recorded at study entry: anthropometrics, type of NMD (listed as Amyotrophic Lateral Sclerosis [ALS] or other NMD, due to peculiar clinical features of ALS), long-term use of home NIV, number of respiratory hospitalizations during the 3 years preceding recruitment, the presence of a cardiomyopathy and/or arrythmia, peak expiratory flow (PEF) and forced vital capacity (FVC) obtained from pulmonary function testing done within about 1 year of recruitment, arterial blood gas results and the presence of pneumonia, fever (temperature>38°C) or leukocytosis (WBC>12,000 x 10^9/L). All patients were followed up until recovery from acute exacerbation, defined as relief of respiratory distress and return of SaO_2 baseline to ≥95% during spontaneous breathing (9). The time to recovery and the vital status at the end of follow-up period were also recorded. For patients of the control group, the time to recovery corresponded to length of hospital stay. Need for hospitalization was recorded for the study group. The vital status at three months from

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acute exacerbation was also determined through telephone calls to patients of both groups.

Intervention

Patients in Group A (study group) were treated according to the following treatment protocol:

A) *Non-Invasive Ventilation:* NIV was delivered at home by a portable ventilator (Trilogy 100 Portable Ventilator, by Philips Respironics, Andover, MA) with single limb circuit and exhalation valve, using the assist/control mode. At the start of the protocol the ventilator was adjusted to obtain a V_T of 10-12 ml/Kg and a respiratory rate of less than 25 breaths/min; the ventilator setting was then readjusted based on measurements of SaO_2, with the goal of maintaining satisfactory gas exchange, that is, $SaO_2 \geq 95\%$. External positive end-expiratory pressure (PEEP) was never added. A full face mask was used on all the patients to start NIV and then, in some cases, substituted by a nasal mask after the first few hours of ventilation. Colloid dressings were placed on the major pressure points to minimize skin injury. NIV was initially delivered continuously, except for brief periods of "rest" (30-60 min), to allow the patients to receive dietary liquid supplements, drink water and speak. After the first 24-48 hrs, if clinical conditions and blood gas exchange were satisfactory, the application of NIV was interrupted by progressively longer intervals of spontaneous breathing. In all cases, nocturnal ventilation via nasal mask was continued until the end of the follow-up period.

B) *Manually and/or Mechanically Assisted Coughing (AC)*: the following techniques were used to improve ability to clear secretions, depending on the patient's clinical status and level of cooperation. a) Manually Assisted Coughing (Man-AC) was employed to provide an optimal insufflation followed by an abdominal thrust in conjunction with the patient's coughing efforts. The portable ventilator was used to deliver the deep

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insufflations. (12). b) Mechanically Assisted Coughing (Mech-AC) was delivered in the presence of stiffness of the chest wall (i.e., severe thoracic deformity or obesity) and to patients unable to fully perform deep insufflation. A mechanical device (Pegaso Cough, by DIMA Italia, Bologna, Italia) was applied via a face mask. The device consists of a two-stage axial compressor that provides positive pressure to the airway, then rapidly shifts to negative pressure, thereby generating a forced expiration. The insufflation and exsufflation pressures and timing were independently adjusted according to efficacy and patient tolerance; generally, pressures between +30 and -40 cm H_2O were applied (8). Typically, a session of assisted coughing was provided whenever the SaO_2 level decreased or the ventilator peak inspiratory pressure increased, or when the patient had an increase in dyspnea or sense of retained secretions. Treatments were usually repeated until one or more of the following were observed: reduction in dyspnea; reduction in respiratory rate; sputum elimination; increased SaO_2 level. Man-AC and Mech-AC were administered for the first three days of the home care protocol by a respiratory therapist who visited the patients each morning and by non-professional caregivers (i.e., the patient's home care attendant or a family member) trained in the application of the device; subsequently, AC was independently administered by home caregivers. The daily treatment frequency was recorded in a diary by district nurses and/or non-professional caregivers.

At the start of treatment protocol, non-professional care attendants received information, instruction and training on cough assistance by respiratory therapists of our Division; training was usually conducted over three consecutive days and consisted of the following: learning how to use NIV, Mech-AC and oximetry; identification of respiratory emergencies; and training in basic life support.

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C) *Continuous SaO_2 monitoring*: patients received pulse oximeters and their caregivers were instructed to perform oximetry feedback (9500 by Nonin, Minneapolis Plymouth) to return SaO_2 to ≥ 95% by assisted coughing or NIV or both as needed.

D) *Antibiotic therapy*: Standard pharmacological treatment was used following guidelines for the management of Acute Bronchitis or Community Acquired Pneumonia (13,14).

E) *Pulmonology visit at home*: a pulmonologist from our team visited the patients each morning for the first three days and thereafter at the discretion of the district nurses or patient's general practitioner, in order to assess the response to therapy and eventually introduce changes.

F) *District nurse visit at home:* a pre-existing service of district nurses visited the patients mornings and afternoons until recovery from acute exacerbation. Nurses assessed the patient's adherence and response to treatment and could request a pulmonology visit if clinical progress was unsatisfactory. The district nurse service included 45 nurses covering an area with a population of approximately 230,000 people and was coordinated by two pulmonologists.

G) *Other interventions*: patient phone access to the pulmonologists of our Division was ensured; patients' general practitioners were faxed to inform them of patients being randomised to the HH program.

The pulmonologist, the nurse, the respiratory therapist and patient could request admission if they felt that clinical progress were unsatisfactory.

Patients in Group B (control group) were admitted to our Division and received usual care consisting of the same drugs and all other supportive measure delivered to the study group, at the discretion of the ward team.

Patients of both groups were administered tracheal intubation and eventually tracheostomy if they developed persistent full-time ventilator dependence and/or worsening respiratory distress and severe hypoxemia.

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Cost calculation

Costs were calculated for each group from the perspective of our Regional Health Service, such that the cost analysis was restricted to direct healthcare costs.

The relevant categories to be considered in order to estimate patient costs were identified as follows: *Study Group A:* 1) home visits by a pulmonologist; 2) home visits by a district nurse; 3) home visit by a respiratory therapist; 4) daily rental costs for mechanical cough assist and portable ventilator; 5) antibiotic prescriptions; and 6) phone calls. *Control Group B:* length of hospital stay.

Data on use of categories were obtained for each patient during the follow-up period.

A second step was the evaluation of resource use. The total cost for each category was calculated as the product of the number of events multiplied by the unit cost per event. Unit costs were expressed as year 2010 prices using Euros. Costs for pulmonology, visits by the respiratory therapist and nurse, antibiotic prescriptions and phone calls were directly calculated using information on labor costs and market prices. The average hospitalization cost per day in the general ward and/or Respiratory Intensive Care Unit (RICU) was available in our hospital.

Study end points and statistical analysis

To assess the efficacy of HH, coprimary study end points were the need for hospitalization for Group A and treatment failure; treatment failure was defined as death or the need for intubation and/or tracheostomy; secondary end-points were time to recovery, death during the first 3 months following exacerbation and the cost of patient care. To our knowledge, our prospective study is the first specifically aimed at investigating the efficacy and safety of a HH model for the management of severe RTIs in NMD patients; as a consequence, the results of any previous study could not be utilized in order to test an *a priori* hypothesis on the expected incidence or magnitude of complication associated with HH, or to estimate an appropriate sample size.

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Standard descriptive statistics were used to illustrate the demographic and clinical characteristics of enrolled patients at baseline. Results were expressed as mean values ± SD, and proportions as appropriate. The independent unpaired Student t test was used to compare continuous variables with normal distribution; nonparametric data were compared using the Mann-Whitney U test. Categorical variables were compared using the $\chi 2$ test or Fisher exact test, when required.

Variables potentially useful in predicting HH failure were analyzed using the Exact logistic regression model, considering that this procedure can adequately estimate a binary response variable with a small sample size; Exact Odds Ratios (OR) were reported for significant values in the univariate and multivariate model (15). The predictor variables of interest included all data recorded at study entry; an exact *p*-value of less than .05 was considered significant.

RESULTS

Fifty-nine consecutive NMD patients were identified as suffering from severe RTI and therefore potentially eligible for the study. Five of the patients were excluded due to their living outside the geographic area followed by our district nurse service and one more since he had declined to undergo intubation and/or CPR by an advance directive; the remaining 53 patients were recruited. Of the 53 recruited patients, 26 were assigned to the study group and 27 to the control group. At baseline, Groups A and B were similar in terms of demographic, clinical and pulmonary function characteristics (see Table 1); however, pneumonia as a cause of acute decompensation was more frequent in patients in Group B (8/26 vs 18/27; p<0.01). Among patients in Group A, 18 (69.2%) responded well, with an uncomplicated course, whilst eight required hospitalization. These eight hospitalized individuals differed from the others in that they were older (66,1 ± 7,7 vs 35,1 ± 16,4 yrs; p<0.0001) and more frequently presented with ALS as baseline disease (7/8 vs 1/18;

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p<0.0001); in addition, they showed a higher number of hospitalizations during the 3 years preceding recruitment (1,63 ± 0,74 vs 0,61 ± 0,7; p<0.05) (see Table 2). With regard to reasons for hospitalization, three patients in Group A required intubation due to persistent mucous encumbrance and severe hypoxemia and subsequently underwent a tracheostomy. Three other patients experienced persistent full-time ventilator dependence and required 24-hour surveillance in our Respiratory Intensive Care Unit (RICU). Two additional patients required insertion of a central venous catheter and infusion of parenteral nutrition, due to insufficient oral food intake.

The outcomes of patients in Groups A and B are compared in Table 3. Treatment failure and time to recovery among patients receiving the HH protocol did not significantly differ from those who were managed in hospital (treatment failure: 8/26 vs 13/27, p=0.19; time to recovery: 8.9 ± 4.6 vs 9 ± 8.9 days p=0.21); in addition, mortality during the 3-month follow-up was similar between the two groups (3/26 vs 4/27 deaths; p=0.42).

By multivariate analysis, HH failure was independently correlated with type of NMD (p=0.0037) with an OR of failure of 17.3 (95% CI, 2.1 to infinity) for patients with ALS. None of the other covariates had any significant effect on HH failure.

Total and daily direct cost of patient healthcare was significantly lower for the 18 patients in Group A who were successfully treated at home compared to hospitalised individuals in Group B (542 ± 258.5 vs 8890 ± 10992.7 euros; p<0.0001 and 65.3 ± 18.6 vs 1060 ± 592.5 euros; p<0.0001, respectively); district nurse service represented the major cost for patients treated at home (320 ± 118.5 euros).

DISCUSSION

This is the first time, to our knowledge, that the efficacy of a HH model in managing NMD patients with RTI has been prospectively evaluated in a controlled study. The major conclusion of our study is that for such patients home hospitalization is as effective as

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conventional hospital care, according to the observation that the proportion of individuals who had a complicated clinical course leading to intubation and/or tracheostomy was similar to that of the hospitalised group and that both time to recovery and mortality at 3-month follow-up did not significantly differ in the two groups. Although a failure rate of approximately 30% for our home-based model may appear to be high, it should be noted that it is in line with previous studies performed in the hospital setting which reported treatment failure in 20 to 50% of patients and concluded that RTIs represent a major cause of morbidity and mortality for this population (16,17).

Even though our HH scheme proved to be effective for most NMD individuals meeting our inclusion criteria, the fact that over one in four of our patients could not be managed in this way and needed hospital treatment does justify our policy of careful home monitoring and makes it necessary to prospectively identify those patients who are at risk of failing at home, in order to adopt appropriate selection criteria. To this aim, we analysed those patient characteristics that were associated with HH failure, and concluded that the type of NMD is of critical importance, with ALS patients doing poorly. In fact, individuals with ALS have a substantially higher risk of HH failure (over 17-fold) compared to those with other NMD and their proportion among patients in Group A who failed HH was significantly greater than among those who responded well. This is in accord with previous reports demonstrating that a non-invasive approach based on NIV and mechanically assisted coughing can be problematic or even ineffective in ALS patients, due to severe bulbar dysfunction leading to an inability to adequately protect the upper airway and severe risk of aspiration of food and saliva (16,18). Our data also show that patients who failed our home-based scheme were significantly older than those who were successfully managed at home: although we cannot exclude that in this group age may be a surrogate for other factors, such as comorbidities, which could have influenced clinical outcome, it must be underlined that concomitant chronic disease has not been found to have a relevant impact

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on the outcome of ALS patients who develop acute exacerbation (19). Finally, we also found that patients who failed HH had a higher hospitalization rate due to a respiratory problem during the last 3 years, supporting the hypothesis that this “frequent exacerbator” phenotype may be considered at high risk of failing home care and require preferential treatment in hospital.

Considering the changes that have occurred in healthcare in the last decade, in particular the emphasis on QoL and cost containment, together with the fact that family members have become an integral part in the home-care of severely disabled NMD patients (20), we were prompted to develop our HH model based on the idea that family caregivers could acquire sufficient knowledge and skill to manage their relatives in case of respiratory complication. Our results show that this new scheme can be effective and that non-professional caregivers can play a critical role in the transition of the care of NMD patients with pulmonary exacerbation from hospital to home, providing complex care to ill relatives, which includes medical and nursing tasks.

In our experience, the average total cost per patient managed by HH was impressively lower than that of conventional hospital care, leading to a cost saving of approximately 8,300 euros per patient. This substantial reduction in healthcare cost, although quantitatively more relevant, is in line with previous studies on home treatment models for such similar conditions as acute exacerbation of Chronic Obstructive Pulmonary Disease and stroke which showed that costs were significantly lower for patients assigned to receive hospital care at home than for those who received inpatient care (21-23). In our study, cost savings can be at least partially explained by the fact that our HH model was essentially carried out by trained family members, leading to a reduction in the cost of labor, which accounts for a large proportion of overall hospital costs and includes salaries for physicians, nurses, technicians, and numerous other personnel (24).

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Some limitations of this study warrant mention. First, data for patient satisfaction and the burden on caregivers were not available; however, it should be noted that the home has been judged to be the ideal environment for NMD individuals receiving respiratory support, since it maintains the independence of the patient and his/her family, thus increasing their QoL (25,26). Second, economic evaluation was conducted from the perspective of our Regional Health Service, such that the cost analysis did not calculate indirect healthcare costs; this is a crucial point, since attendant care by the family represents approximately 88% of the total cost for assisting ventilated individuals at home (27).

CONCLUSIONS

Despite its limitations, we believe that our study provides useful information for physicians caring NMD patients, in terms of clinical practice, which can be summarised as follows:

- hospital at home, with involvement of family or other properly trained nonprofessional caregivers as partners in the management of the disease, is a safe and effective option for selected NMD patients developing severe RTI;
- patients with ALS should not be included in a HH model, since they have a high chance of failing at home; physicians should preferentially consider conventional hospital care for this population when RTI arises;
- HH is likely to prove extremely useful in substantially reducing costs compared to traditional hospitalisation.

Based on these considerations, we believe that effort should be expended to transform the management of RTI in NMD individuals from a hospital-centered to a home-centered treatment, with the caveat that proper selection of patients remains critical.

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	Group A	Group B	P Value
Number of subjects	26	27	-
Sex (males, females)	17, 9	24, 3	NS
Age, yrs	44.6 ± 20.4	46.7 ± 20.2	NS
BMI	21.4 ± 6.5	21.8 ± 4.2	NS
Type of NMD (ALS, other)	8,18	13,14	NS
Pts previously administered long-term NIV, N	20	24	NS
N. hospitalizations in 3 yrs	1.04 ± 1.02	1.00 ± 1.02	NS
Pts with cardiomyopathy and/or arrythmia, N	7	9	NS
FVC, L	1.42 ± 1.01	1.22 ± 0.83	NS
PEF, L/s	2.77 ± 2.05	2.28 ± 1.36	NS
PaO_2 , mmHg	69.2 ± 6.7	66.8 ± 7	NS
$PaCO_2$, mmHg	48.8 ± 4.5	51.8 ± 5.9	NS
SaO_2 (%)	93.7 ± 2.4	93.3 ± 2.9	NS
Pts with hypercapnia, N ($PaCO_2$> 45mmHg)	19	21	NS
Pts with pneumonia, N	8	18	<0.01
Pts with fever, N (Temperature>38°C)	14	13	NS
Pts with leukocytosis, N (WBC>12,000 x 10^9/L)	12	12	NS

Table 1: Anthropometric, clinical, pulmonary function and blood gas data at study entry of patients treated by the HH model (Group A) or hospitalised (Group B).

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	Pts successfully treated at home	Pts requiring hospital admission	P Value
Number of subjects	18	8	-
Sex (males, females)	13, 5	4, 4	NS
Age, yrs	35,1 ± 16,4	66,1 ± 7,7	<0.0001
BMI	19,8 ± 7	24,9 ± 3,4	NS
Type of NMD (ALS, other)	1,17	7,1	<0.0001
Pts previously administered long-term NIV, N	15	5	NS
N. hospitalizations in 3 yrs	0,61 ± 0,7	1,63 ± 0,74	<0.05
Pts with cardiomyopathy and/or arrythmia, N	7	-	NS
FVC, L	1,3 ± 0,93	1,68 ± 1,2	NS
PEF, L/s	2.49 ± 1.8	3.42 ± 2.6	NS
PaO_2 , mmHg	69.8 ± 6.1	68.9 ± 8.3	NS
$PaCO_2$, mmHg	49.5 ± 4.5	47.1 ± 4.2	NS
SaO_2 (%)	93.9 ± 2.2	93.1 ± 3	NS
Pts with hypercapnia, N ($PaCO_2$> 45mmHg)	14	5	NS
Pts with pneumonia, N	3	3	NS
Pts with fever, N (Temperature>38°C)	8	4	NS
Pts with leukocytosis, N (WBC>12,000 x 10^9/L)	7	5	NS

Table 2: Anthropometric, clinical, pulmonary function and blood gas data at study entry of patients in group A who were successfully treated by the HH model or required admission to hospital.

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	Group A	Group B	P Value
Pts who required hospitalisation, N.	8	-	NA
Treatment failure, N.	8	13	NS
Time to recovery (days)	8.9 ± 4.6	9 ± 8.9	NS
Death at 3-month follow-up, N	3	4	NS
Total cost of patient care, euros	542 ± 258.5	8890 ± 10992.7	<0.0001
Daily cost of patient care, euros	65.3 ± 18.6	1060 ± 592.5	<0.0001

Table 3: Outcomes and direct cost of healthcare of patients treated by the HH model (Group A) or hospitalised (Group B). For patients of group B, time to recovery corresponded to length of hospital stay.