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Carme Hernandez, RN, MSc, Jesús Aibar, Dr, Jordi de Batlle, PhD, David Gomez-Cabrero, PHD, Nestor Soler, Dr, Enric Duran-Tauleria, Dr, Judith Garcia-Aymerich, Dr, Xavier Altimiras, Dr, Monica Gomez, Mrs, Alvar Agustí, Dr., Joan Escarrabill, Dr, David Font, Dr, Josep Roca, Prof

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ASSESSMENT OF HEALTH STATUS AND PROGRAM PERFORMANCE IN PATIENTS ON LONG-TERM OXYGEN THERAPY

Carme Hernandez, MSc[1,6], Jesús Aibar Dr[1], Jordi de Batlle PhD[2], David Gomez-Cabrero PHD[3], Nestor Soler Dr[1], Enric Duran-Tauleria Dr[4], Judith Garcia-Aymerich Dr[4], Xavier Altimiras Dr[5], Monica Gomez Mrs[1], Alvar Agustí Dr.[1], Joan Escarrabill Dr[1,6], David Font Dr[1], Josep Roca Prof[1] and the NEXES consortium

Affiliations:

1. Hospital Clinic de Barcelona, CIBER en Enfermedades Respiratorias (CIBERES); Institut d'Investigacions Biomèdiques August Pi i Sunyer (IDIBAPS), Universitat de Barcelona. Catalonia. Spain.
2. International Agency for Research on Cancer (IARC), Lyon, France.
3. Unit of Computational Medicine, Department of Medicine, Center for Molecular Medicine, Karolinska Institutet, Karolinska University Hospital, Sweden.
4. Centre de Recerca en Epidemiologia Ambiental (CREAL), CIBER en Epidemiologia y Salud Pública (CIBERESP); Department of experimental and Health Sciences, Universitat Pompeu Fabra, Barcelona, Catalonia. Spain.
5. Consorci Sanitari de Barcelona. Servei Català de la Salut. Generalitat de Catalunya.
6. Master Plan for Respiratory Diseases (PDMAR), Ministry of Health and REDISSEC (Research Network in Chronic Care). Barcelona. Catalonia. Spain.

Corresponding author: Carme Hernandez, RN, MsC. Atenció Integrada, Hospital Clínic; Universitat de Barcelona; IDIBAPS; CIBERES; Barcelona, Spain. Villarroel 170, 08036 Barcelona, Spain. Tel: 34-93-2279368, Fax: 34-93-2275455, E-mail: chernan@clinic.ub.es

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ABSTRACT *(n=232)*

Background: Despite well established clinical guidelines, performance of long-term oxygen therapy (LTOT) programs shows marked variability among territories. The current study assessed the LTOT program and the health status of patients on LTOT prior to the deployment of community-based integrated care in an urban health district of Barcelona (Spain).

Aims: To assess: *i)* the LTOT program and health status of the patients on LTOT in the health district; *ii)* their frailty profile; and, *iii)* the requirements for effective deployment of integrated care services for these patients

Methods: Cross-sectional observational study design including all patients (n=406) on LTOT living in the health district. Health status, frailty, arterial blood gases, forced spirometry and hand-grip muscle strength were measured. Network analysis of frailty was carried out.

Results: *Adequacy of LTOT prescription* (n=362): 47% and 31% of the patients had PaO_2≤60 mmHg and ≤55 mmHg, respectively. *Adherence to LTOT:* 31% of all patients used LTOT ≥15h/d; this figure increased to 67% in those with PaO_2≤60 mmHg. *Assessment of frailty:* Overall, LTOT patients presented moderate to severe frailty. *Care complexity* was observed in 42% of the patients.

Conclusions: Adequacy and adherence to LTOT was poor and many patients were frail and complex. The outcomes of the network analysis may contribute to enhance assessment of frailty in LTOT patients. These observations suggest that an integrated care strategy has the potential to improve the health outcomes of these patients.

Key words: Continuous oxygen therapy, Adequacy; Adherence; Chronic patients; Frailty; Integrated Care.

INTRODUCTION

Integrated Care has demonstrated a remarkable potential to enhance health outcomes and contain economic costs[1] in chronic patient management. This requires the efficient transfer of care complexities from hospital-based specialized care to the community. A key learning observation in the deployment process undertaken in Barcelona[1] was the need to formulate and assess community-based integrated care services (ICS) for frail chronic patients.

The current study was prompted by the hypothesis that patients on Long-Term Oxygen Therapy (LTOT) may present requirements that could be efficiently covered by community-based ICS with potential to improve LTOT outcomes and raise healthcare efficiencies[2].

It is of note that current clinical indications and logistics for administration of LTOT are based on the results of two classical studies carried out, in patients with Chronic Obstructive Pulmonary Disease (COPD), more than three decades ago[3;4] Moreover, despite well defined clinical guidelines on LTOT[5-8], there are deficits in LTOT indications and administration, as well as large variability among programs[9]. It is assumed that all these issues could be better addressed within an integrated care scenario.

As a baseline evaluation, prior to the deployment of ICS in the health district, we: *(1)* assessed the adequacy of prescription and the adherence to LTOT of all patients receiving LTOT in one of the urban health districts of Barcelona (Barcelona-Esquerra, 540.000 inhabitants) in Spain; *(2)* characterized comprehensively their health status, frailty, care complexity and use of healthcare resources; and, *(3)* applied network analysis to examine the

associations among different dimensions of frailty and their impact on health-care use. The results of the study should provide the basis for the design of a novel integrated care service for these patients to be prospectively evaluated during 2015[10].

METHODS

Study Design and Ethics

This cross-sectional observational study enrolled all patients older than 40 years of age on prescribed LTOT in Barcelona-Esquerra (Spain) according to the Catalan Health Care (CatSalut) single-payer registry. The regional LTOT is highly regulated, but both prescription and follow-up are done on a conventional care basis which implies fragmentation of information and care. Hospital-based specialized physicians, pulmonologists or internists, can prescribe LTOT and respiratory specialists are responsible for LTOT follow-up *(see additional organizational details in the on-line supplementary* material). Standard LTOT eligibility criteria were applied[3;4]. Briefly, LTOT prescription was adequate in clinically stable patients with optimal medical therapy showing $PaO_2 \leq 55$ mmHg breathing room air or patients in the grey area regarding PaO_2 that present at least one of the following conditions: poliglobulia; pulmonary hypertension (cor pulmonale); or oxygen desaturation (≤ 85%) during exercise. The study protocol was approved by the Ethics Committee of the 3 hospitals attending patients in Barcelona-Esquerra (Hospital Clinic, Hospital Sagrat Cor and Hospital Plató). All participants signed their informed consent.

Patient characterization

Patient characterization was carried out at the patient's home by nurses and physiotherapists duly trained for the study in 3 sequential home visits of 40 minutes each during 3 weeks, and included **(Table 1S):** *(1)* a standardized interview and self-administered questionnaires*(see on line document for details)*; *(2)* arterial blood gas measurement[11], *(3)* forced spirometry[12], (4) hand-grip muscle strength quantification[13], as displayed in (**Figure 1**). Additional information was obtained from patient electronic health records following the current legislation on access and confidentiality of the clinical data. The information was grouped into five dimensions according to the structure proposed by WHO[14] to describe the characteristics of chronic patients, namely: *i)* socio-demographics*; ii)* health team and system related factors; *iii)* characteristics of patient's chronic conditions; *iv)* risk factors and treatment; and, *v)* patient dependence factors.

Frailty is a multifactorial condition defined as a clinical state in which there is augmented individual's vulnerability for developing increased dependency and/or mortality when exposed to a stressor[15]. The patient characterization included different variables potentially related to frailty (see **Table 3S** in the on-line supplementary material) beyond factors expressing disease severity. The frailty variables, as described in detail in the on-line supplementary material ***(see text and Tables 1S, 2S.1 and 2S.2)*****,** were allocated in all five WHO dimensions alluded to above. We used the comprehensive frailty score Canadian Scale of Health and Aging (CSHA)[16] as one of the dimensions assessed in the study. An individual results report was shared with the patient and his/her attending physician.

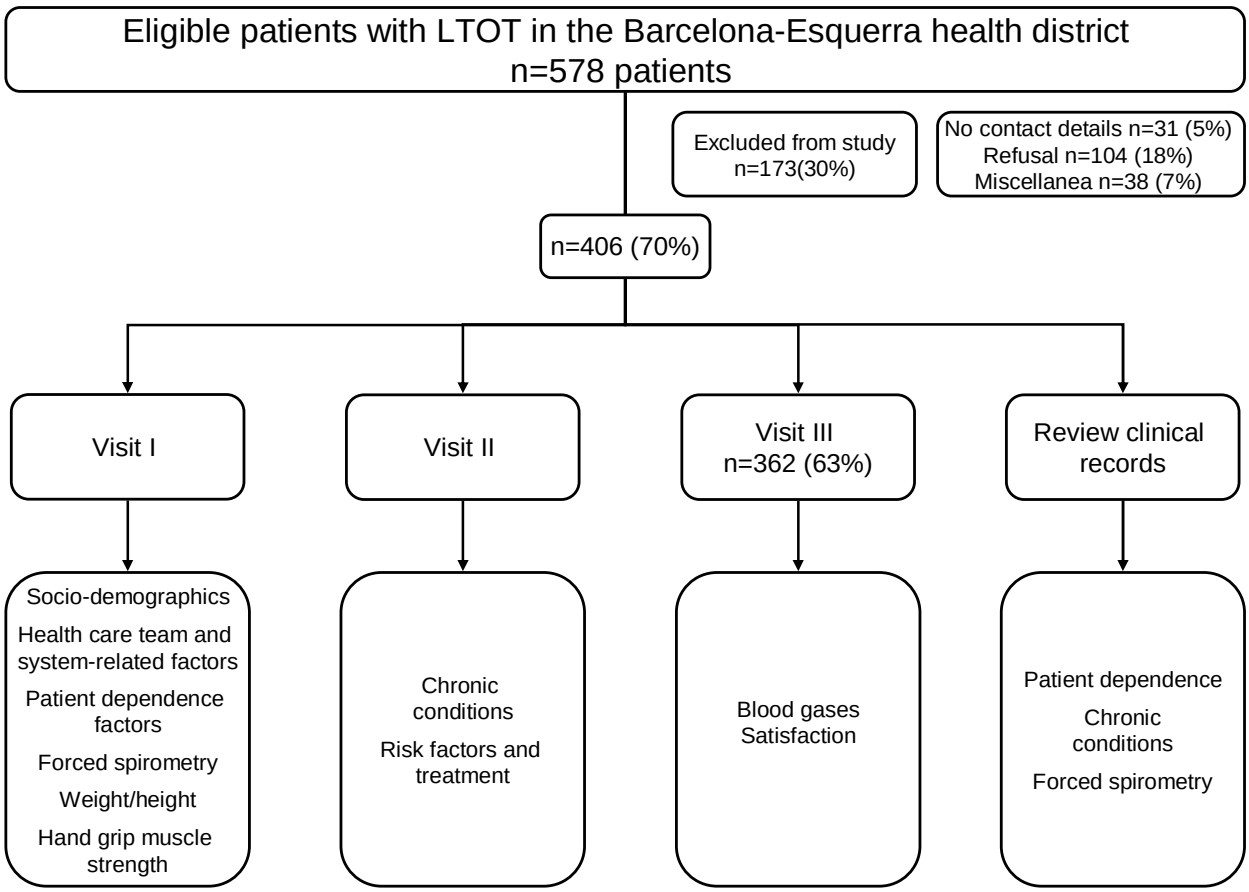
Statistical analysis

Results were expressed as mean and standard deviations (SD), medians (p25-p75), absolute number or percentages (%), as appropriate. Analyses of the characteristics of the distributions of the different variables were carried out and statistical tests for bi-variate comparisons and assessment of associations were chosen accordingly. Crude and adjusted logistic regression models were constructed for analysis of covariates associated to LTOT adherence as dependent variable. All variables showing statistical significance in the corresponding bi-variate assessment, as well as other particularly relevant variables according to published literature, were included in the final logistic models. Then, multivariate models were constructed using a backward stepwise method (considering a significance level for removal of 0.20 and a significance level for inclusion of 0.15), combined with accurate handling of multi-collinearity among variables (pruning). The goodness of fit of all the models was assessed using the Hosmer-Lemeshow test[17] We also conducted a network analysis to investigate the associations among the different dimensions of frailty with relevant (continuous or ordinal) variables of the study. The network was generated by first computing non-parametric Spearman correlations; then correlations found to be statistically significant after Benjamini-Hochberg[18] adjustment for multiple testing (adjusted p-value<0.05) were used to construct the network. Finally, Cytoscape[19] was used to visualize the constructed network (Edge-Weighted Force-Directed Layout algorithm). All these analyses were conducted using Stata 10 program (StataCorp, College Station, TX, USA) and R[20].

RESULTS

Patient characteristics

Figure 1 presents the Consort diagram of the study.



Of the initial 578 recipients of LTOT in the health district, 173 (30%) were excluded from the analysis because they either refuse to participate (n=104, 18%), could not be localized (n=31, 5%) or suffered a miscellaneous of causes for exclusion (n=38, 7%). Excluded patients (n=173, **Figure 1**) included more females (p<0,001), had a higher Charlson Index (p<0,001), and required more intensive care admissions (p=0,024), but had similar age and history of hospital admissions in the previous two years, than patients included in the analysis. **Tables 1,** ***2S-1*** and ***2S-2*** present a detailed description of the socio-demographic, clinical characteristics and frailty together with information on use of healthcare resources of the 406 patients finally included in the study, which is further discussed below. According to spirometry results, 50% of participants (n=203) had chronic obstructive pulmonary disease (COPD): GOLD III, 31%; and, GOLD IV, 55%. The main diagnoses in the remaining 50% LTOT patients were distributed as follows: diagnosis of COPD without support of forced spirometry (n=80, 20%); advanced cardiac disease (n=33, 8%); c) restrictive pulmonary diseases (n=24, 6%); d) hypoventilation-obesity (n=17, 4%); e) bronchiectasis (n=16, 4%); and, f) cancer-palliative care (n= 33, 8%).

Table 1. **Socio-demographic and clinical characteristics of the study group** (n=406)

Socio-demographic	
Age (m, SD)	76±10
Social aspects:	
APGAR Index (median, p25-75)	10(8-10)
Institutionalization risk (median, p25-75)	7(4-10)
Health care team and system-related factors	
Public health coverage (%)	97
Some type of health Insurance (%)	23
Using public health care system in the last 2 years (%)	89
Chronic condition	

One or more chronic conditions (n, %)	281(70)
Number of chronic conditions (median, p25-75)	3(0-5)
Charlson Index modified by age(m, SD)	5±2
Risk factors and treatment	
Smoking (n, %)	
Active smokers	1(0)
Ex-smokers	283(70)
Never	122(30)
Body Mass Index (BMI) (m, SD)	28±7
Physical Activity (n, %)	
Sits most of the day	329(81)
Walks twice or three times a week for at least 30 minutes	175(43)
Pharmacological treatment nº different treatments (median, p25-75)	9(7-12)
CPAP/BIPAP (n, %)	50(13)
Inhaler therapy (n, %)	332(85)
Self-monitoring techniques (median, p25-75)	1(1-2)
Poor adherence to treatment (Morinski-Green) (n, %)	3(1)
Patient's dependence factors	
Quality of life (SGRQ). Total (m, SD)	53±14
Clinical frailty scale. Canadian Study Health Aging (CSHA)	
Severely frail (4-6) (n, %)	270(67)
Terminally ill (7-8) (n, %)	39(10)
Anxiety and depression (HAD) (n, %)	
Anxiety (moderate/clinic)	142(35)
Depression (moderate/clinic)	171(42)

Mean (SD), median (p25-p75) or number (%) were used for the description of variables. The Family APGAR. Family function (Adaptability, Partnership, Growth, Affection, Resolve), Continuous Positive Airway Pressure (CPAP), Bi-level positive airway pressure (BIPAP), St. George Respiratory Questionnaire (SGRQ). See table **1S** for information on scores of the variables and **tables 2S-1 and 2S-2** in the online supplementary material for further details on the parameters measured in each patient

Adequacy of LTOT prescription and adherence

Arterial blood gases were measured in 63% of participants (n=362), and arterial PO_2 was ≤55 mmHg in 31% and ≤60 mmHg in 47% of them. LTOT adherence, defined as LTOT use for ≥15 hours per day, was 31%; it increased to 67% in patients with PaO_2 ≤60 mmHg. Accordingly, only patients with PaO_2 ≤60 mmHg (n=168) were considered for the bi-variate analysis of adherence to LTOT displayed in **Table 2.**

Table 2. Comparison between LTOT patients with PaO_2 ≤60 mmHg (n=168) **with adherence to therapy (≥15h/d)** (n=113) **and those with poor adherence** (n=55)

	Poor adherence (n=55)	**Adherence** (n=113)	**p-value**
Socio-demographic			
Occupational status			0.030
Health care team and system-related factors			
Use of healthcare resources during the previous 2 years			
Hospital			
Visit to emergency room, n(%)	27(52)	40(36)	0.049
Number of respiratory admissions (median, 25-75)	0(0-0)	0 (0-1)	0.034
Primary care			
Doctor visit	6(2-10)	2(1-4)	0.045
Nurse visit	0(0-4)	0(0-0)	0.045
Chronic conditions			
FEV_1 (l)	1.04(0.50)	0.76(0.41)	0.003
FVC (l)	2.10(0.94)	1.67(0.75)	0.015
PO_2 mmHg	53.3(5.3)	50.3(6.9)	0.003
PCO_2 mmHg	46.2(7.7)	51.3(8.9)	<0.001
≥ 1 chronic conditions	2(0-4)	4(0-6)	0.034
Dyspnea: MRC	3(2.5-4)	4(3-4)	0.044
Risk factors and treatment			
Walk at least 30 min two or three times a week	57	43	0.044
Dependence factors			
Barthel Index	85(21)	76(25)	0.016
Quality of life (SGRQ)			
Activity	64(22)	77(20)	<0.001
Impact	40(14)	46(15)	0.007
Symptoms	44(17)	53(19)	0.003
Total	48(13)	56(14)	<0.001
CSHA			0.019

Mean (SD), median (p25-p75) or number (%) were used for the description of variables. Forced expiratory volume (FEV_1); Forced vital capacity (FVC); Partial pressure of oxygen (PO_2)Partial pressure of carbon dioxide (PCO_2) ; Medical Research Council (MRC); Disability profile scale (Barthel Index); St. George Respiratory Questionnaire (SGRQ); Clinical frailty scale. Canadian Study Health Aging (CSHA). See table **1S** for information on scores of the variables and **tables 2S-1 and 2S-2** in the online supplementary material for further details on the parameters measured in each patient.

Briefly, patients with poor adherence showed: *i)* higher use of healthcare resources; *ii)* less disease severity assessed by lung function impairment, symptoms and co-morbidities; *iii)* higher physical activity; and, *iv)* less dependence, lower frailty score and better health-related quality of life. The multivariate analysis confirmed that poor LTOT adherence was significantly

associated with higher use of health care resources both in Primary Care and at the Hospital level, and that this was unrelated with disease severity assessed either by either arterial blood gases, forced spirometry or the Charlson index[21].

Frailty Analysis

The overall picture displayed in **Table 1** indicates that LTOT patients indicate moderate frailty. Patient social requirements were reasonably covered by their families jointly with the social support services, yet some unmet needs associated to frailty were detected, namely: *i)* Thirteen percent of the patients showed markers suggesting high risk for institutionalization, *ii)* poli-pharmacy was important, mean of 9 (7-12) drugs, *iii)* physical barriers limiting mobility were evident in 21% of the LTOT patients; and, *iv)* Charlson index[21] was elevated, 5±2. As indicated in Methods, a detailed description of variables that contribute to frailty was done in the on-line supplementary material (**Table 3S**).

Briefly, socio-demographic analysis showed that 67% of patients (n=273) were older than 75 yrs. and that most lived with a caregiver of similar age. The assessment of healthcare related factors indicated that the majority of patients (74%, n=313) followed regular hospital-based outpatient specialized visits, at least every 3-6 months, and visited different types of specialists (range 1 to 3). Only 17% (n=69) of the patients indicated that they followed regular follow-up by primary care professionals. During an episode of exacerbation, 78% of the patients were self-referred to an emergency department and, only 7% (n=30) referred participation, at least once, in educational programs for chronic conditions. The results of the assessment of co-morbidities, poli-pharmacy and major risk factors for chronic conditions, as well as different dimensions of dependence are detailed in **T2S.1** and **T2S.2**. The most prevalent co-

morbidities identified in the clinical records were: heart disorders ((39%), arterial hypertension (27%), Type II diabetes (16%), obesity (12%), cancer (12%) and sleep apnoea (10%), Moreover, anxiety-depression was assessed in approximately 40% of the patients.

It is of note that according to CSHA[16] criteria, severe frailty was present in 67% of the cases. Ten percent of the patients were qualified as end-stage cases defined as individuals fully dependent on carers for the activities of daily living and/or terminally ill (life expectancy < 6 months).

Healthcare Resources Utilization

Forty three per cent of participants (n=172) did not require hospitalization during the previous 2 years, 21% (n=85) had one admission and the remaining 36% (n=142) needed ≥2 admissions during the 2 years period. **Table 3** compares the characteristics of patients with (one or more) and without a previous history of hospitalizations. Patients with history of admissions during the previous year had worse health-related quality of life (p<0.001), more co-morbidities (p<0.001), higher Charlson index (p<0.001), required more visits at home by the primary care nurse (p<0.001) and presented worse health-related quality of life (SGRQ) (p<0.001) than those admission-free.

Table 3. Comparison between LTOT patients with history of hospital admissions in the previous 2 years and LTOT hospital-free patients

	Hospital admission (n=234)	**Hospital free** (n=172)	**p-value**
Socio-demographic			
Educational level (n,%)			<0.001
None	15(7)	3(2)	
Primary school	164(75)	112(62)	

Secondary school	40(18)	65(36)	
Institutionalization risk (median, p25-75)	7(5-10)	7(4-9)	0.027
Health care team and system-related factors			
Routine management of other chronic diseases (n, %)	154(41)	108(59)	0.018
To whom you address questions about your respiratory illness? (n, %)			0.014
Primary Care	85(39)	41(23)	
Specialist. Outpatient Clinic/Day Hospital	44(20)	44(25)	
Emergency room	15(7)	8(4)	
Others	62(28)	70(39)	
Where do you go during an episode of exacerbation? (n, %)			<0.001
Emergency department	162(74)	107(60)	
Primary Care	26(12)	13(7)	
Respiratory specialist. Outpatient Clinic/Day Hospital	13(6)	12(7)	
Others	17(7)	47(27)	
Use of healthcare resources during the previous 2 years			
Hospital			
Emergency room visits, n (%)	147(84)	27(16)	<0.001
Outpatient			
Primary care visit (doctor)	13.5(7-23)	9(1.5-12)	0.004
Primary care visit (nurse)	5(3-8)	1(0-3.5)	<0.001
Respiratory specialist visit	2(0-5)	0(0-0)	0.002
Emergency room visits	7(3-13)	1(0-2.5)	<0.001
Chronic conditions			
Number co-morbidities (median, p25-75)	4(3-7)	0(0-3)	<0.001
Charlson Index modified by age (m, SD)	6±2	4±2	<0.001
Risk factors and treatment			
Smoking (packs/year) (median, p25-75)	66(40-96)	51(31-85)	0.026
LTOT ≥15hours/day (n, %)	82(39)	88(51)	0.024
Knowledge of the disease (n, %)	167(76)	117(65)	0.014
Dependence			
Quality of life (SGRQ)			
Symptoms (m, SD)	53±19	46±19	<0.001
Anxiety and depression (HAD)			
Anxiety (m, SD)	7±5	6±4	0.002
Depression (m, SD)	8±5	7±4	0.012
Self-efficacy (m, SD)	24±7	25±8	0.018

Mean (SD), median (p25-p75) or number (%) were used for the description of variables. Long term Oxygen Therapy (LTOT); St. George Respiratory Questionnaire (SGRQ); Hospital anxiety and depression scale (HAD). See table **1S** for information on scores of the variables and **tables 2S-1 and 2S-2** in the online supplementary material for further details on the parameters measured in each patient.

Respiratory Care Complexity

In the Barcelona-Esquerra health district, shared-care agreements across levels of care state that respiratory specialists take direct responsibility in the management of those patients showing care complexity besides LTOT, namely: *i)* patients with non-invasive mechanical ventilation; *ii)* nebulized antibiotics; *iii)* patients with complex co-morbid conditions with history ≥ 3 hospital admissions

in the last year; and, *iv)* end-stage complex disease. The remaining patients should be managed in the community. According to these criteria, 42% of LTOT patients in our study (n=172) required management by specialized respiratory care whereas the remaining 58% can be managed at community level with access to the specialist through primary care professionals when needed.

Network analysis

Figure 2 displays the network of significant associations among the variables included in the analysis.

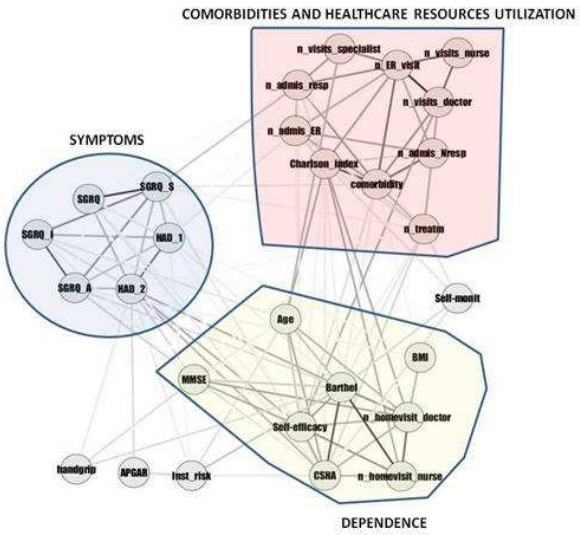


Figure 2. Network analysis displaying the associations between different dimensions of frailty and with the use of healthcare resources. The level of bi-variate associations is represented by the intensity of the spectrum of grey shades, from white (Rho=0.12) to black (Rho=0.80), of the connexions between variables. The cluster labelled as *symptoms* displays correlations among health-related quality of life (SGRQ) and anxiety-depression scores. A second cluster indicated as *co-morbidities and healthcare resources utilization* shows associations between comorbidity-associated variables, number of treatments, and use of healthcare resources during exacerbation episodes. The third cluster, *dependence,* includes pivotal variables describing the degree of patient's autonomy, namely: Barthel index, CSHA, minimental test, self-efficacy that

show a logical association with the number of home visits by Primary Care professionals. It is of note that physical frailty (hand-grip muscle strength), Apgar score and risk of institutionalization did not show relevant associations with any of the 3 modules. Only variables showing statistical significance (adjusted p-value<0.05) using non-parametric Spearman correlation, after adjustment for multiple-testing were represented in the network *(see Table 3S in the on-line supplementary material for detailed information on correlations)*.

That is, the dimensions of frailty assessed in the study and the use of healthcare resources. Despite that most of them were low to moderate **(Figure 2 and *Table 3S*),** we identified three well-defined clusters that we labelled as*: i) Symptoms; ii) Dependence; and, iii) Co-morbidities and Healthcare Resources Utilization (see the legend of **Figure 2** for further details)*.

DISCUSSION

The results of this study provide a detailed picture of the characteristics of patients on LTOT in the health district of Barcelona-Esquerra in Spain, and generate potentially valuable information on their health status, frailty and care complexity, as well as on their major patterns of use of healthcare resources. Specifically, the study provides evidence of: *i)* suboptimal LTOT prescription and adherence; *ii)* hospitalization rate of LTOT patients, which are below average figures both in the Catalan region and those reported both at Spanish and European levels for chronic respiratory patients[22-24]; *iii)* high use of specialized outpatient care resources together with underuse of primary care resources; and, *iv)* the network structure of the different dimensions of frailty with the identification of three well-defined modules: Symptoms, Co-morbidities and Dependence.

We understand that the research provides the basis for the design of an enhanced LTOT program in our area that should be assessed in a future longitudinal study. Such an approach will overcome some limitations of the

current analysis due to the high percentage of patients (30%) no included in the current analysis.

Prescription and Adherence to LTOT

Despite a tightly regulated LTOT prescription in place in our region since the mid-90s[25], both adequacy of the prescription and adherence to LTOT determined in the current study were low. This is similar to previous observations in other European countries[8;26-28]. However, in areas where in specific LTOT policies, beyond a tight regulation, have been adopted; the quality of the service has significantly improved over time. This is the case of Sweden[7;9;29-32] that: (i) created a national registry administered by the Swedish Respiratory Society, (ii) enforced an innovative workflow, and, (iii) generated 9 indices for longitudinal evaluation of LTOT. They have generated positive outcomes that contributed to increase the interest on LTOT[2;7;8;33].

The initial assessment of arterial blood gases triggering LTOT prescription might have been suboptimal (and we cannot check this due to fragmentation of health-care information), either because it was not carried out in clinically stable patients after hospital discharge or simply because arterial blood gases were not taken into account despite the tight regional regulation in place. Another potential explanation for the low adequacy of LTOT prescription may be biological changes of PaO_2 over time enforcing the need for periodic checking of PaO_2 assessment in LTOT patients. In any case, the results of our study highlight the need for: *i)* a rigorous validation of the initial LTOT prescription following standard of care guidelines[6], *ii)* periodic assessments of the prescription in non end-stage patients; and, *iii)* ICT-supported organizational interoperability that facilitates the accessibility to information and collaborative

work among actors across healthcare tiers, as described elsewhere[1]. All in all, these observations support the development of new paradigms[1] that: *(i)* enhance the adequacy of prescription by generating information useful to refine the rules for indication of LTOT in patients located in the "grey area" for eligibility of the therapy[1;5], *(ii)* consolidate recommendations for transient indication of LTOT in some patients; and, *(iii)* empower patient self-management. The positive outcomes generated by the use of the personal health folder in ICT-supported integrated care deployment projects[34] strongly advice to explore its use in targeted patients to enhance LTOT adherence.

Healthcare Resources Utilization

Our study identified some areas with a high potential for generation of healthcare efficiencies with a care coordination approach in these patients. We observed that the regular follow-up of chronic conditions in approximately 74% of the study group relied on hospital-based outpatient specialized care with clear under use of primary care resources. Only 17% of the LTOT patients used primary care and we observed an almost negligible deployment of preventive strategies including patient empowerment for self-management. Moreover, despite LTOT patients did not present an abnormally high rate of severe episodes of exacerbation requiring hospitalization as indicated above, they self-referred too often to the emergency room department for the management of episodes of exacerbations. Different studies analyzing determinants of hospitalization in LTOT patients stress the importance of co-morbidity[30;35;36] as displayed in **Figure 2** of the current study. It is of note that hospital-free patients

(**Table 3**) presented better health-related quality of life (SGRQ score) and lower rate of nurse visits at home than those with history of hospitalizations.

Respiratory Care Complexity

We observed that a majority of LTOT patients (58%), because of their level of care complexity, were candidates for community-based management. This indicates that a proper articulation between community-based care strategies and specialized respiratory care may generate health care efficiencies. To this end, an ICS, including transactions across healthcare tiers with ICT support[1] of organizational interoperability among all actors (specialists, primary care professionals, patients and relatives, informal care providers, payer, social workers and homecare companies, etc.) appears as a sustainable solution. Recent reports assessing Complex Care Management seem to support the above statement[37].

Network analysis of frailty dimensions

The network analysis evaluated several dimensions of frailty using well-validated questionnaires. We acknowledge that the assessment of the physical component of frailty was limited to the measurement of hand-grip muscle strength. In any case, to the best of our knowledge, this is the first study that investigates the network structure relationships of the different frailty dimensions **(Figure 2).** Using this approach, we identified three well-defined modules (Symptoms, Co-morbidities and Dependence) with associations of variables that seem to provide the rationale for enhanced characterization and management of frailty. These results reinforce the expected associations

between disease and frailty dimensions. However, further research exploring the effects of specific interventions tailored to these clusters is warranted.

The different ongoing initiatives that foster deployment of integrated care for chronic patients[1;10;38] acknowledge that assessment of frailty is a necessary component for a proper patient-based health risk evaluation and stratification. The latter constitutes one of the basic components to establish shared-care arrangements across healthcare tiers. However, a recent report by Kim Bouillon et al[39] reviewing an extensive number of frailty scales, up to 27, concluded that none of them is accepted as a gold standard. Consequently, an operational definition of frailty for use in healthcare should be recognized as an unmet need that was beyond the scope of the current study. We believe that the network analysis strategy followed in the current study has generated a relevant contribution for the design of the enhanced LTOT program to be assessed in a future longitudinal study.

Implications of findings for the health-care system

Overall, the results of this study support the need of a novel integrated care service (ICS) for LTOT patients (LTOT_ICS) with two objectives: *i)* optimize LTOT prescription and adherence; and, *ii)* enhance community-based patient management according to the frailty profile/network observed in these patients. **Table 4** summarizes the major lessons learnt and high-level proposals for the design of such LTOT_ICS.

Table 4. Proposals for the design and implementation of a novel integrated care service (ICS) for patients with long-term oxygen therapy (LTOT_ICS)

1. Consolidation of the main LTOT_ICS objectives, namely: integrated management of both LTOT and frailty/complexity of the patient; and enhanced LTOT outcomes.
2. Identification of actors, roles, standard transactions among actors and required technological support for the novel service.
3. Proposals for subject-specific risk assessment and stratification
4. BPMN representation of the LTOT_ICS.
5. Identification of CDSS.
6. Generation of the new LTOT_ICS into the existing ICT-platform.
7. Identification and development of enhanced functionalities to be integrated into the ICT-platform to support the novel service.
8. Further developments of the ICT-platform to enhance current support of organizational interoperability at systems level.
9. Design of the long-term assessment methodology during the deployment of the novel service and beyond.
10. Implementation of novel reimbursement modalities.

Long term Oxygen Therapy (LTOT); Integrated Care Service (ICS); Clinical decision Support Systems (CDSS); Information and Communication Technology (ICT); BPMN, Business Process Modelling Notation.

Likewise, *Figure 1S* presents an initial proposal of this LTOT_ICS using the business process management notation (BPMN)[40] formalism. We propose that three major requirements are needed in order to ensure adoption of this novel LTOT_ICS, namely: *i)* ICT support to organizational interoperability at the health care system level that includes both formal and informal care; *ii)* rigorous long-term assessment using comparative effectiveness research approach[41]; and, *iii)* implementation of novel reimbursement modalities, as recommended in[1].

Finally, we would like to propose that this LTOT_ICS might be transferrable to other chronic conditions associated to frailty. The novel integrated care service should be in place within 2015 and it will be closely assessed during one-year follow-up. Both the results of the current study and prospectively collected indicators from the LTOT program at regional level will be use as controls. Moreover, the longitudinal study will serve to select appropriate indicators for long-term assessment of the ICS_LTOT.

Limitations of the study

Well identified limitations of the current study were: *(i)* the high percentage of patients not included in the analysis (30%); and, *(ii)* the cross-sectional nature of the study design using retrospective information for analysis. The latter precluded the use of modelling approaches for risk assessment, but, overall, the main messages and conclusions of the study were not significantly constrained by these limitations. Moreover, the study intentionally did not address specificities of LTOT that require further research. We acknowledge that the current results should constitute the basis for a longitudinal design aiming at evaluating the proposals generated in the study. Such an initiative is already in place as part of the policies undertaken to foster adoption of novel integrated care services for chronic patients at regional level[10] .

Conclusions

The results of the current research indicate the need for improving adequacy of LTOT prescription, as well as for enhancing adherence to the therapy with special focus on patients with less severe disease. Moreover, the study

identifies potential for generating health efficiencies through an integrated care approach.

Authors' contributions

CH, designed, initiated and supervised the field study. Moreover, and contributed to the elaboration of the manuscript; JA made a major contribution in the field study and preparation of the logistics of the database, JB performed the statistical analysis; DG performed the network analysis; NS, made major contributions to the field study; ED participate to perform the questionnaires and data base; JG had a major role in the methodology of the study and data interpretation; XA was instrumental for the realization of the study at community level and reviewed the manuscript; MG, was instrumental for the realization of the study at community level and reviewed the manuscript; AA generated major scientific and editorial contributions; JE generated major scientific and editorial contributions; DF was instrumental for the realization of the study; JR was the NEXES coordinator and contributed to the writing of the manuscript a gave the final approval of the version to be published. All authors have been involved in the elaboration of the manuscript, reading and approving the final version. All authors contributed equally.

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Competing interests No competing interests have been identified.

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ASSESSMENT OF HEALTH STATUS AND PROGRAM PERFORMANCE IN PATIENTS ON LONG-TERM OXYGEN THERAPY

Carme Hernandez[1,5], Jesús Aibar[1], Jordi de Batlle[2], David Gomez-Cabrero[3],Nestor Soler[1], Enric Duran-Tauleria[2], Judith Garcia-Aymerich[2], Xavier Altimiras[4], Monica Gomez[1], Alvar Agustí[1], Joan Escarrabill[1,5], David Font[1], Josep Roca[1] and the NEXES consortium

On-line supplementary material

Introduction

The current document is structured as follows. Firstly, it provides the definition and scores of relevant variables used in the analysis (Table 1S). Followed by an expanded description of the characteristics of the study group (Tables 2S.1 and 2S.2) highlighting the dimensions of frailty assessed in the study.

Organization of LTOT during the study period – As described in the main manuscript, the study was done in a conventional care scenario. The prescribing centers had the equipment necessary to perform arterial blood gas analysis. Such a test is required to prescribe LTOT. Also, prescription of a portable oxygen source requires performance of a walking test. A respiratory physician visited the patients at 3 m after prescription (outpatient visit for LTOT) and every year thereafter, but specialized nurses were not involved in the workflow. At the time of the study, there was not interoperability between LTOT registry and electronic health records, nor with social support services. Moreover, mobile technologies were not used in the conventional clinical practice.

As indicated in the main manuscript, the information reported in Tables 2S.1 and 2S.2 was grouped using the structure proposed by WHO[1] to describe the characteristics of chronic patients including 5 dimensions, namely: *i)* socio-demographics*; ii)* health team and system related factors; *iii)* characteristics of patient's chronic conditions; *iv)* risk factors and treatment; and, *v)* patient dependence factors.

The information on frailty dimensions is complemented by a detailed report (Table 3S) on bi-variate non-parametric correlations done as part of the network analysis. It is of note that all variables in Tables 2S.1 and 2S.2 were included in the network analysis of frailty, but Figure 2, in the main manuscript, and Table 3S, in the current document, only display those variables showing statistical significance ($p<0.05$) after adjustment for multiple comparisons.

Finally, Figure 1S displays a first approach to the novel Integrated Care Service (ICS) for patients with Long-Term Oxygen Therapy (LTOT_ICS) represented using the Business Process Management Notation (BPMN) formalism[2].

Extended description of patient characteristics and frailty dimensions

1. *Socio-demographics* – Patients (39% women) were elderly (67% with ≥ 75 yrs, n=273) living with a caregiver of the same age. Thirty-nine per cent (n=158) had some type of external support for home-based daily life activities. In 21% (n=85) of the cases were identified architectonic barriers to access the home that generated significant limitations in terms of patient mobility.

Key dimensions of frailty under socio-demografics were the Apgar test[3] and risk of institutionalization. The former[3] assesses the level of support in the family environment. Its results indicated that 10% (n=41) of the patients showed moderate problems in terms of family support and only 5% (n=20) clearly displayed unmet needs requiring external social support. Regarding the risk of institutionalization, we identified that 13% (n=53) of the patients showed markers indicating high dependence and risk for institutionalization. In 8% (n=32), the risk was associated to combined healthcare and social unmet needs, whereas the remaining 5% (n=20) showed only social factors as determinants of the risk for institutionalization.

2. *Healthcare related factors* indicated that a vast majority of patients (74%, n=313) followed regular hospital-based outpatient specialized visits, at least every 3-6 months, visiting different types of specialists (range 1 to 3). They indicated that chronic conditions were routinely controlled only at hospital level in 59% of the cases. Only 17% (n=69) of the patients indicated a regular follow-up of their chronic disorders by primary care professionals. During an episode of

exacerbation, 78% of the patients are self-referred to an emergency department, only 10% contacted the primary care professional and the remaining 12% contacted programs run by the Integrated Care Unit. Moreover, only 7% (n=30) referred participation, at least once, in coaching programs for chronic conditions. It is of note, however, that both patients and caregivers showed a high level of satisfaction regarding the quality of healthcare, ranging from 71-97%, depending upon the type of service. The use of healthcare resources was included in both the logistic regression analysis of covariates of hospital admission and in the network analysis, as shown in Table 3S.

3. *Characteristics of patient's chronic conditions* and 4. *Risk factors and treatment* - The results of the assessment of co-morbidities, poli-pharmacy, care complexity and major risk factors for chronic conditions are displayed in Tables 2S- and 2S-2 Briefly, 70% have at least one or more chronic conditions[4], the Charlson Index[5] modified by age was 5±2. The most prevalent co-morbid conditions being: cardiovascular disorders (39%), obesity (12%), cancer (12%) and sleep apnoea (10%). Hand-grip muscle strength[6] was moderately low in 49% of the patients and severely impaired in 8% of them. The prevalence of patients with low body mass index[7] was only 3%, but obesity was seen in 35% of the patients; whereas overweight was also observed in 35% of the cases. Sedentarism was a prominent feature in the study group: 81% of the patients were sitting at home most of the day and only 43% (n=175) did light to moderate outdoors activity only once or twice a week[8].

In 80% (n=325) of the patients, the source of oxygen was a static concentrator, with continuous flow that was portable in 97 patients, 24% of the entire LTOT group, whereas oxygen liquid was used in the remaining 20% (n=81) of the patients. In 13% (n=53) of the patients, LTOT was delivered together with other respiratory therapies providing non-invasive ventilatory support, namely: CPAP (Continuous Positive Airway pressure) or BIPAP (Bilevel Positive Airway Pressure).

5. *Dimensions of dependence* using: *i)* Barthel Index[9], severely altered in 16% of the patients; *ii)* minimental test[10], abnormal mental status[10] detected in 22% of the patients; *iii)* health-related quality of life[11], total score 53±14; and, *v)* assessment of anxiety and depression scores[12] (severely altered in 19% and 24% of the patients, respectively) showed an overall picture indicating a moderate degree of dependence for the entire study group. All these variables were pivotal dimensions in the assessment of frailty. The assessment of self-efficacy in terms of management of the chronic conditions showed acceptable results (24±7). The comprehensive CSHA frailty score[13] detected severe frailty in 67% of the cases and 10% of the patients were qualified as end-stage cases. But the limited discriminative power of CSHA between moderate and severe levels of frailty is widely accepted.

TABLE 1S. Definitions and scores

	Measurements	Scores
Adequacy and adherence[14-17]		
Adequacy *(test)*	Arterial blood gas analysis	PaO_2 < 55mmHg (7.3 kPa) or PaO_2 ranging from 56- 59mmHg (7.4–7.8 kPa) in the presence of cor pulmonale, hematocrit >55% or exercise-induced hypoxemia <85%
Adherence *(patient interview)*		≥ 15 hours/day
Analysis of frailty		
Socio-demographic		
Family function and institutionalization risk	APGAR Index[3] Risk of institutionalization	Score (no dysfunction 7-10; moderate: 4-6;.severe 0-3) Score (no risk <11; social intervention 11; social-health care risk >11) The need for a caregiver was defined when the patient was functionally dependent (Barthel Index <60) and/or cognitively impaired (PQ≥3 errors)
Chronic conditions and risk factors		
COPD diagnosis	Forced spirometry[18]	FEV_1/FVC <0.70
Co-morbidities	Charlson Index adjusted by age[5]	Co-morbidities (ICD9-CM codes). Main and secondary chronic diagnoses (in case of repeated admissions, only de last one was evaluated)
Risk factors	Body mass index[7]	Score: (low :< 18 Kg/m^2; normal: 18-24.9 Kg/m^2; overweight: 25-29.9 Kg/m^2; obesity: ≥30 Kg/m^2)
	Hand grip muscle strength[6]	Males (in Kg):(60-64 yrs (weak <30.2; normal 30.2-48-0; strong > 48.0)); (65-69 yrs (weak <28.2; normal 28.2-44.0; strong >44.0)); (70-99 yrs (weak <21.3; normal 21.3-35.1; strong > 35.1)) Females (in Kg): (60-64 yrs, (weak <17.2; normal 17.2-31.0; strong > 31.0)); (65-69 yrs (weak <15.4; normal 15.4-27.2; strong >27.2)); (70-99 yrs (weak <14.7; normal 14.7-24.5; strong >24.5))
Treatment complexity[19]	Self-monitoring techniques	Total number of treatments Total number of self-monitoring techniques
Treatment adherence	Morinski-Green questionnaire[20]	If at least one of the answers is YES the patients is classified as having poor adherence
Patient's dependence factors		
Functional dependence	Barthel Index[9]	Score: (100 autonomous; 60 moderate; 40-55 severe; <20 total)
Mental evaluation	Mini-mental test[10]	Score: (24-30 normal; 20-30 slight; 10-19 moderate; 0-9 severe)
Quality of life	SGRQ[11]	Score: (0-100, with higher scores indicating more limitations)
	CSHA[13]	Score: (1 (robust health); 7 (complete functional dependence on others))
Anxiety and depression	HAD[12]	In a scale ranging from 0 to 21: 0 to 7 normal range;, 8-10 Grey area –undefined diagnosis; ≥11 probable anxiety and/or depression
Self-efficacy	General sense of perceived self-efficacy[21]	Score: Responses are made on a 4-point scale. Sum up the responses to all 10 items to yield the final composite score with a range from 10 to 40.

Long term Oxygen Therapy (LTOT); Partial pressure of oxygen in arterial blood (PaO_2); The Family APGAR. Family function (Adaptability, Partnership, Growth, Affection, Resolve), Cognitively impaired (mini-mental test); Disability profile scale (Barthel Index); Chronic Obstructive Pulmonary Disease (COPD); Forced expiratory volume in one second/ forced vital capacity (FEV_1/FVC); Age, dyspnoea, and airflow obstruction (ADO Index); Adapting a clinical comorbidity index for

use with administrative databases (ICD9-CM). St. George Respiratory Questionnaire (SGRQ); Clinical frailty scale. Canadian Study Health Aging (CSHA); Hospital anxiety and depression scale (HAD).

Table 2S.1. Socio-demographic, health care team & system-related factors (n=406)

Socio-demographic *(patient interview)*	**Value**
Age (m, SD)	76±10
APGAR Index (median p25-75)	10(8-10)
Functional (n,%)	345(85)
Mild (n,%)	41(10)
Seriously (n,%)	20(5)
Institutionalization risk (median, p25-75)	7(4-10)
No risk (n,%)	352(87)
Social intervention (n,%)	20(5)
Social health care risk (n,%)	34(8)
Health care team and system-related factors *(patient interview and clinical record)*	
Some type of health insurance, (%)	23
Use of the public health care system in the last 2 years (%)	89
Routine control for respiratory illness (n,%)	
Every 3-6 months	300(74)
One time per year	41(10)
Never	57(14)
Specific control for oxygen therapy (n,%)	140(34)
Blood gases control (n,%)	
Every 6 months	98(25)
Every year	102(26)
Only during a visit in the Emergency room or Hospitalization	164(40)
Never	35(9)
Home Care programs (n, %)	280(69)
Primary Care	110(42)
Hospital	110(42)
Palliative Care	14(5)
Others	30(11)
Hospital resources (2008-09)	
Emergency room visits (n,%)	174(44)
Number of emergency room visits (median, p25-75)	0(0-1)
One or more admissions for respiratory problems (n,%)	138(35)
One or more admissions for NON respiratory problems (n,%)	145(36)
Intensive Care Unit visit (n,%)	27(12)
Primary Care resources (2008-09)	
Outpatient visits by doctor (median, p25-75)	11(4-17)
Outpatient visits by specialist (median, p25-75)	0(0-4)
Outpatient visits by nurse (median, p25-75)	3(0-7)
Home visit by nurse (median, p25-75)	0(0-2)
Home visit by doctor (median, p25-75)	0(0-1)
Emergency room visits (median, p25-75)	3(1-7)

Mean (SD), median (p25-p75) or number (%) were used for the description of variables. The Family APGAR. Family function (Adaptability, Partnership, Growth, Affection, Resolve). See table **1S** for information on scores of the variables.

Table 2S.2. Chronic conditions, risk factors and dependence factors (n=406)

Chronic condition *(patient interview and clinical record)*	**value**
≥ 1 chronic conditions (n,%)	281(70)
Number of comorbidities (median p25-75)	3(0-5)
Charlson Index modified by age (m,SD)	5±2
Risk factors and treatment *(patient interview and clinical record)*	
Smoking	
Active smokers (n,%)	1(0)
Ex-smokers (n,%)	283(70)
Never	122(30)
Body Mass Index (BMI) (m,SD)	28±7
Low weight (n,%)	11(3)
Normal (n,%)	105(27)
Overweight (n,%)	130(35)
Obesity (n,%)	130(35)
Alcohol intake (n,%)	113(28)
Physical Activity (n,%)	
Sits all day	329(81)
Walks twice or three times a week for at least 30 minutes	175(43)
Hand strength (n,%)	
Normal	172(43)
Decreased	195(49)
Highly altered	30(8)
Number of pharmacological treatments (median, p25-75)	9 (7-12)
CPAP/BIPAP (n,%)	50(13)
Inhaler therapy (n,%)	332(85)
Self - monitoring techniques (median, p25-75)	1(1-2)
Poor adherents to treatment (Morinski-Green) (n,%)	3(1)
Patient's dependence factors *(self-administrated questionnaires)*	
Barthel Index (m,SD)	78±24
Autonomous (n,%)	99(22)
Moderate dependency (n,%)	250(62)
Severe dependency (n,%)	26(6)
Total dependency (n,%)	40(10)
Mini-mental test (m,SD)	28±7
Quality of life (SGRQ) (m,SD)	
Activity	71±22
Impact	44±14
Symptoms	50±19
Total	53±14
CSHA (n,%)	
Good (1-3)	97(24)
Severely frail (4-6)	270(66)
Terminally ill (7-8)	39(10)
Anxiety and depression (HAD) (n,%)	
Anxiety (normal)	264(65)
Anxiety (moderate/clinic)	142(35)
Depression (normal)	235(58)
Depression (moderate/clinic)	171(42)
Self-efficacy (m,SD)	24±7

Mean (SD), median (p25-p75) or number (%) were used for the description of variables; Long term Oxygen Therapy (LTOT); Continuous Positive Airway Pressure (CPAP), Bilevel positive airway pressure (BIPAP); Disability profile scale (Barthel Index); St. George Respiratory

Questionnaire (SGRQ); Clinical frailty scale. Canadian Study HealthAging (CSHA); Hospital anxiety and depression scale (HAD). See table **1S** for information on scores of the variables

	Self-efficacy	CSHA	Barthel	HAD_1	HAD_2	APGAR	Inst_risk	SGRQ	SGRQ_S	SGRQ_A	SGRQ_I	MMSE	BMI	handgrip	n_treatm	Inhaler	Self-monit	n_admis_resp	n_admis_Nresp	comorbidity	Charlson_index	n_admis_ER	n_visits_doctor	n_visitis_specialist	n_visits_nurse	n_homevisit_nurse	n_homevisit_doctor	n_ER_visit	Age
Self-efficacy	406	####	####	####	####	0,06	####	####	####	####	####	####	0,09	####	####	0,06	####	####	####	####	####	####	####	####	0,02	####	####	####	####
CSHA	406	406	0,57	0,14	0,32	0,06	0,18	0,17	0,18	0,23	0,05	0,14	####	0,07	0,22	####	0,20	0,08	0,12	0,11	0,17	0,10	0,11	0,02	####	0,32	0,32	0,02	0,34
Barthel	406	406	406	0,16	0,34	0,06	0,27	0,11	0,09	0,21	####	0,26	####	0,21	0,19	####	0,22	0,09	0,12	0,16	0,16	0,08	0,12	0,09	####	0,60	0,42	0,13	0,28
HAD_1	406	406	406	406	0,46	0,11	0,15	0,36	0,27	0,27	0,31	0,08	0,01	0,11	0,12	0,03	####	0,13	0,12	0,12	0,09	0,17	0,13	0,08	####	0,22	0,11	0,00	####
HAD_2	406	406	406	406	406	0,21	0,17	0,30	0,28	0,28	0,19	0,23	####	0,17	0,14	0,01	0,10	0,08	0,08	0,08	0,02	0,03	0,03	0,11	####	0,29	0,23	####	0,06
APGAR	406	406	406	406	406	406	0,23	0,01	0,05	0,01	####	0,02	0,05	0,00	0,00	0,05	0,00	0,05	0,01	####	0,01	####	####	####	####	####	####	####	####
Inst_risk	406	406	406	406	406	406	406	0,03	0,03	0,10	####	0,11	####	0,03	0,03	0,03	0,00	####	0,05	0,05	0,11	0,02	0,06	0,09	####	0,08	0,14	####	0,20
SGRQ	406	406	406	406	406	406	406	406	0,63	0,83	0,87	####	####	0,09	0,10	0,11	####	0,13	0,05	0,08	0,03	0,09	####	0,11	0,02	0,12	####	0,09	####
SGRQ_S	406	406	406	406	406	406	406	406	406	0,39	0,43	0,04	####	0,10	0,15	0,10	####	0,26	0,12	0,18	0,09	0,11	0,04	0,21	####	0,06	####	0,25	####
SGRQ_A	406	406	406	406	406	406	406	406	406	406	0,52	####	####	0,12	0,06	0,05	####	0,06	0,03	0,05	0,05	0,04	####	####	0,07	0,13	####	####	0,08
SGRQ_I	406	406	406	406	406	406	406	406	406	406	406	####	####	0,01	0,06	0,11	####	0,09	0,01	0,03	####	0,08	####	0,12	####	0,08	####	0,09	####
MMSE	406	406	406	406	406	406	406	406	406	406	406	406	0,05	0,21	0,04	####	0,09	0,12	0,04	0,13	0,08	0,05	0,24	####	####	0,25	0,37	0,18	0,18
BMI	376	376	376	376	376	376	376	376	376	376	376	376	376	####	0,11	####	0,00	0,04	0,04	0,15	####	0,09	0,07	####	####	0,25	0,31	0,03	####
handgrip	397	397	397	397	397	397	397	397	397	397	397	397	367	397	0,00	0,01	####	0,03	0,03	0,02	####	####	0,03	0,14	####	0,19	0,17	0,13	####
n_treatm	389	389	389	389	389	389	389	389	389	389	389	389	361	381	389	0,07	0,18	0,14	0,12	0,29	0,19	0,21	0,30	0,15	0,08	0,13	0,13	0,26	0,06
Inhaler	389	389	389	389	389	389	389	389	389	389	389	389	361	381	389	389	####	####	####	####	####	0,02	0,17	####	0,15	####	####	0,23	####
Self-monit	221	221	221	221	221	221	221	221	221	221	221	221	205	217	221	221	221	0,09	0,15	0,15	0,19	0,13	####	####	####	0,22	0,03	0,02	####
n_admis_resp	399	399	399	399	399	399	399	399	399	399	399	399	370	390	384	384	217	399	0,12	0,37	0,19	0,29	0,14	0,34	0,24	0,16	0,21	0,39	####
n_admis_Nresp	399	399	399	399	399	399	399	399	399	399	399	399	370	390	384	384	217	399	399	0,47	0,27	0,34	0,32	0,12	0,15	0,24	0,13	0,31	####
comorbidity	399	399	399	399	399	399	399	399	399	399	399	399	370	390	384	384	217	399	399	399	0,54	0,34	0,38	0,15	0,17	0,20	0,12	0,47	0,01
Charlson_index	399	399	399	399	399	399	399	399	399	399	399	399	370	390	384	384	217	399	399	399	399	0,21	0,20	0,02	0,03	0,33	0,32	0,34	0,32
n_admis_ER	399	399	399	399	399	399	399	399	399	399	399	399	370	390	384	384	217	399	399	399	399	399	0,27	0,10	0,25	0,07	0,25	0,31	####
n_visits_doctor	71	71	71	71	71	71	71	71	71	71	71	71	67	71	68	68	41	70	70	70	70	70	71	0,24	0,48	0,13	0,20	0,64	0,00
n_visitis_specialis	71	71	71	71	71	71	71	71	71	71	71	71	67	71	68	68	41	70	70	70	70	70	71	71	0,20	0,03	0,02	0,41	####
n_visits_nurse	71	71	71	71	71	71	71	71	71	71	71	71	67	71	68	68	41	70	70	70	70	70	71	71	71	####	0,16	0,48	####
n_homevisit_nurs	71	71	71	71	71	71	71	71	71	71	71	71	67	71	68	68	41	70	70	70	70	70	71	71	71	71	0,51	0,21	0,29
n_homevisit_doct	71	71	71	71	71	71	71	71	71	71	71	71	67	71	68	68	41	70	70	70	70	70	71	71	71	71	71	0,28	0,31
n_ER_visit	71	71	71	71	71	71	71	71	71	71	71	71	67	71	68	68	41	70	70	70	70	70	71	71	71	71	71	71	####
Age	406	406	406	406	406	406	406	406	406	406	406	406	376	397	389	389	221	399	399	399	399	399	71	71	71	71	71	71	406

Table 3S. Matrix of Spearman correlations (rho) including all variables used in the network analysis (the n of cases for each variable is indicated in the diagonal line, see main manuscript for further details). Self-efficacy (General sense of perceived self-efficacy[21]); CSHA[13] (Canadian study of Health and Ageing); Barthel Index[9] (Functional dependence); HAD[12] (Anxiety and Depression); APGAR Index[3] (Family function and institutionalization risk); SGRQ[11] (St.George Respiratory Questionnaire): MMSE (Mini-mental test[10]); BMI[7] (Body Mass Index); nhandgrip (value); n treatm (number of different pills.); Inhaler (number of inhalation per day); Self-monit (number of self-monitoring thecniques); n-admis resp (admissions for respiratory problems); n-admis_Nresp (admissions for non respiratory problems); comorbidity (number of comorbidities); Charlson Index adjusted by age[5] (Comorbidity-Adjusted Life Expectancy); n_admis_ER (number of emergency room visits); n_visits doctor (number of times the patient visits a doctor (Primary Care); n-visits-specialist (number of times the patient visits a specialist in the Primary Care center)); n_visit-nurse (number of times the patient is visited by a nurse (Primary Care); n_home visit_nurse (number of times the patient is visited by a nurse (Primary Care); n_homevisit_doctor (number of times the patient is visited by a doctor (Primary Care); n_ER-visit (number of times the patient visits an Emergency Room (Primary Care).

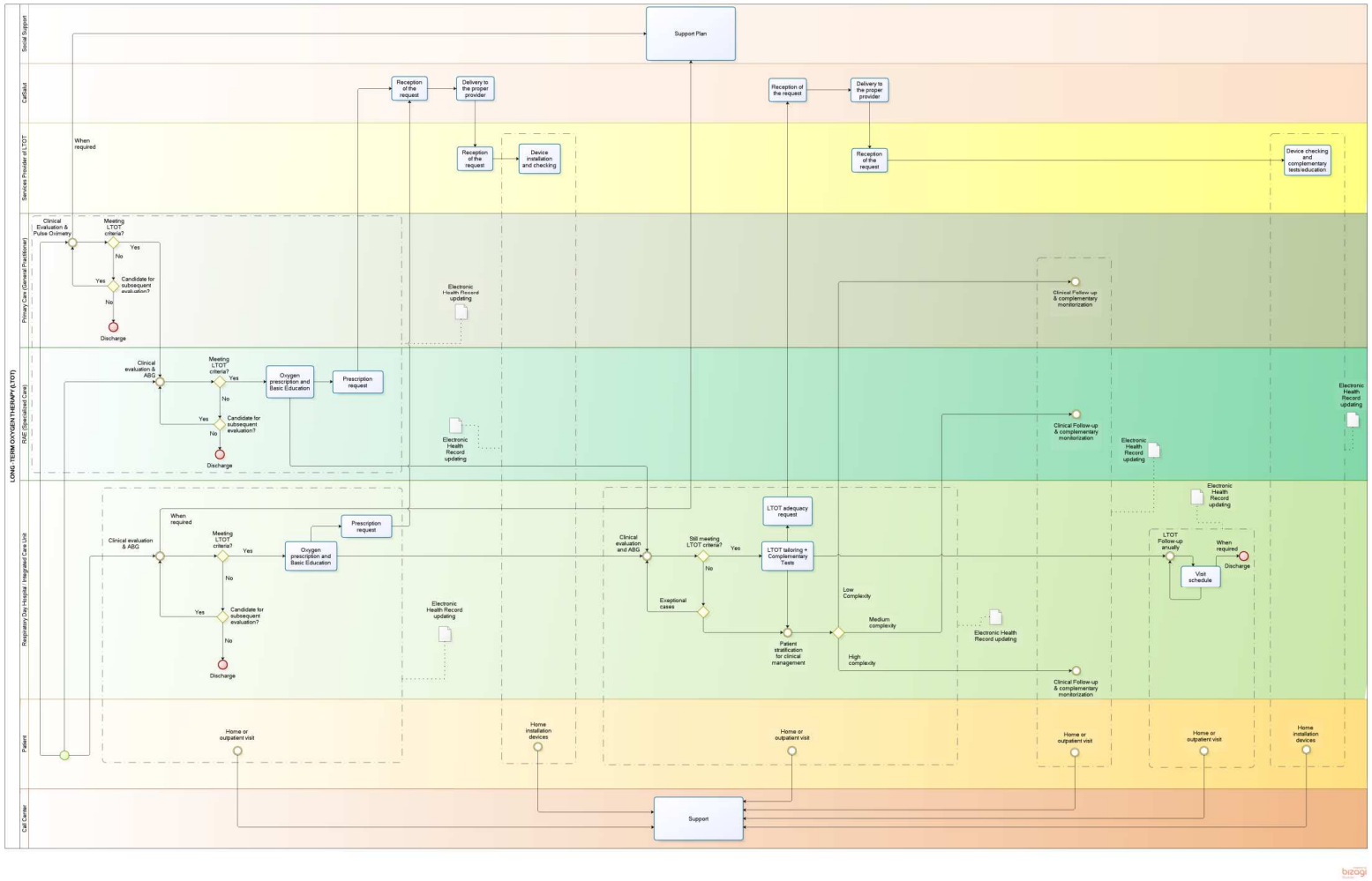

Figure 1S- Integrated Care Service for LTOT patients (LTOT_ICS) described using the Business Process Modeling and Notation (BPMN) formalism

FIGURE LEGENDS

Figure 1S- Integrated Care Service for LTOT patients (LTOT_ICS) described using the Business Process Modeling and Notation (BPMN). RAE refers to the reform of specialized care in the territorial care scenario. It indicates specialized support to primary care physicians. CatSalut refers to the single public payer agency in the Catalan health system. The current BPMN formalism is oriented to LTOT management in an integrated care scenario. However, management of other patient care needs may require further developments of the current BPMN description

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