STUDY TITLE

Title: ProMuscle Study. Clinical Trial on the use of a protein module enriched with Hydroxymethylbutyrate (HMB) in patients with deficient protein intake and/or increased protein requirements.

Protocol code: ProMuscle2025

STUDY RESPONSIBLE PERSONS

Names, titles, degrees, specialty, place of work and addresses of all responsible persons, including the coordinating investigator (if there are several centres), with a list of all primary collaborating entities and other relevant study locations:

Dr. José Manuel García Almeida. Head of the Nutrition Unit, Virgen de la Victoria University Hospital (Málaga) (Principal Investigator)
Ms. Isabel María Vegas Aguilar (Collaborating Investigator)
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Ms. Mar Amaya Campos (Data Manager)

Version 1.0 of March 18, 2025

Nutritional status and body composition are key determinants in the health and functionality of the individual, particularly in patients with chronic disease or accelerated aging. Disease-related malnutrition (DRE) is defined as an imbalance between energy and nutrient intake and requirements, which generates adverse metabolic and functional changes, affecting patients' quality of life, functional capacity, and morbidity and mortality【1】. Among the determining factors in the progression of DRE and sarcopenia is inadequate protein intake and/or increased protein requirements, resulting in a progressive loss of muscle mass and decreased strength, contributing to frailty and deterioration of physical functionality【2】.

Protein deficiency can be due to multiple factors, including reduced intake, malabsorption, or pathological conditions that increase metabolic demand. Various studies have shown that protein insufficiency leads to loss of muscle mass, decreased strength, and impaired physical function, which affects the patient's independence and increases the risk of clinical complications【3】. The mechanisms involved in this process include increased muscle catabolism, reduced protein synthesis, and alterations in the signaling of the mTOR pathway, which regulates muscle growth【4】. In patients with chronic kidney disease (CKD), inflammation and metabolic acidosis aggravate protein degradation and promote muscle atrophy, exacerbating malnutrition and muscle dysfunction.【1】
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The diagnosis of functional and structural loss of muscle requires the integration of assessment tools that allow an accurate characterization of the patient's condition. The evaluation of muscle strength by manual dynamometry has been widely validated as a prognostic marker of sarcopenia and malnutrition, in addition to being a reliable predictor of morbidity and mortality【4】. Other functional tests, such as the Timed Up and Go (TUG) and squat tests, allow the mobility and responsiveness of the lower body to be assessed, which facilitates the identification of individuals at risk【3】. At the same time, the quantification of muscle mass using techniques such as electrical bioimpedance (BIA) and vector bioimpedance (BIVA) has become relevant in the characterization of nutritional status, allowing the estimation of the skeletal muscle mass index (ASMI), the muscle mass index (SMI) and the phase angle, the latter considered an independent marker of cell quality and nutritional status【5】. In a complementary way, nutritional ultrasound has proven to be an emerging tool in the evaluation of muscle mass, with the rectus femoris as a reference site for the assessment of muscle involvement in patients at risk of malnutrition【2】.

Given the evidence that supports the importance of adequate protein intake in the preservation of muscle mass and function, various strategies have been proposed to optimize nutrition in patients with increased requirements. The use of oral nutritional supplements (ONS) and protein modules has been shown to be effective in improving strength and body composition parameters, contributing to the preservation of functionality【6】. Within these, the administration of high-quality protein and branched-chain amino acids (RAAs), especially leucine, has been one of the most studied strategies for its role in activating protein synthesis through the mTOR pathway【3】. In this context, **β-hydroxy-β-methylbutyrate (HMB),** an active metabolite of leucine, has been extensively researched for its anabolic and anti-catabolic properties. Its mechanism of action includes the activation of the mTOR pathway, favoring protein synthesis, and the inhibition of muscle degradation pathways, such as the ubiquitin-proteasome system and lysosome-mediated autophagy【7】.

A recent meta-analysis by **Prado et al. (2022)** evaluated the effects of HMB supplementation in cancer patients, a population characterized by a high prevalence of muscle loss and functional impairment. The analysis included **15 studies** (six randomized clinical trials and nine observational studies) in which different formulations of HMB were administered, primarily in combination with essential amino acids or as part of oral nutritional supplements. The results indicated that in the studies of higher methodological quality, HMB supplementation had a beneficial effect **on the preservation or increase of muscle mass** in four of the four studies analyzed, while improvements in **muscle function were reported in two out of two studies**. In addition, a reduction in the duration of hospitalization and the rate of readmissions was observed in three out of three studies, while five out of seven studies reported a positive impact on the **survival** of patients supplemented with HMB. However, the effects on quality of life and body weight maintenance were not consistent. Importantly, **no serious adverse effects associated with HMB supplementation were reported**, supporting its safety and tolerability in this population.【8】

These findings reinforce the evidence that HMB could represent an effective therapeutic strategy in preserving muscle mass and function, especially in individuals with increased requirements or at risk of accelerated muscle loss. However, given the heterogeneity of the available studies, well-designed clinical trials are required to confirm these benefits in populations with different clinical profiles.

The objective of this study is to evaluate the efficacy and tolerance of an HMB-enriched protein module in the improvement of muscle function, body composition

and nutritional status in patients with insufficient protein intake and/or increased requirements. It is proposed that the administration of this supplement will preserve muscle mass and improve functional parameters compared to the standard dietary intervention, representing an effective nutritional strategy in the optimization of the clinical status of these patients.

Working hypothesis

The implementation of an HMB-enriched protein module for patients with protein intake deficit and/or increased protein requirements improves functional, muscular and/or nutritional parameters, with high tolerance and safety, compared to standard dietary intervention.

RESEARCH OBJECTIVES

General objective

To evaluate the efficacy and tolerance of a protein module in improving functional, muscular, and/or nutritional parameters in patients with deficient protein intake and/or increased protein requirements.

Specific objectives

1. To evaluate changes in physical functionality measured by hand dynamometry and quadriceps dynamometry, for the evaluation of strength, and the *Timed Up and Go Test (TUG), squats (STS), and 20 increment in maximum repetition (20RM).*
2. To estimate the effect of protein modulus on muscle mass in terms of preservation and/or improvement of lean mass by ultrasound of the anterior rectus quadriceps (nutritional ultrasound) and vector electrical bioimpedance analysis (BIVA).
3. To assess the effect of protein modulus on the reduction of disease-related malnutrition (assessed by GLIM criteria) and on the reduction of sarcopenia (assessed by EWGSOP 2).
4. Analyze tolerance to the product, including possible adverse effects.
5. To analyze adherence to treatment using quantitative methods of recall, dispensing record and qualitative method (Wanden-Berghe adherence test).

Type of study

Study design

Prospective, randomized, open-label, two-parallel, and PHASE IV (post-marketing) clinical trial. The study will evaluate the efficacy and tolerability of an HMB-enriched protein module for patients with increased protein requirements and/or deficient protein intake. The protocol ensures that:

- Assignment to the intervention group will be random and will be done using a computerized system.
- The dispensing of the protein module will be carried out within a normal clinical setting, without interfering with the prescribing habits of the treating physician or the dispensing procedures of the pharmacist.

Environment

Adult patients (≥18 years old) with deficient protein intake and/or increased protein requirements attended at the specialized endocrinology and nutrition service of the Virgen de la Victoria University Hospital in Malaga.

Study Period

Recruitment will take place over 6 months, and each participant will be followed over a period of 3 months with a schedule of visits: baseline visit, intermediate (telephone) visit, final visit.

Inclusion Criteria:

- Adult patients (≥18 years old).
- Patients with increased protein requirements
- Patients who meet nutritional risk criteria and do not meet protein needs
- Patients who are able to perform functional tests
- Patients who sign the informed consent.

Exclusion Criteria:

- Severe or decompensated comorbidities (e.g., class III-IV heart failure, decompensated COPD, decompensated DM).
- Known allergy to module components.
- Participation in another clinical trial at the time of inclusion.
- Patients with an active regimen of supplementation and/or modules enriched with HMB.

Sample size

Sample size calculation

To determine the sample size of the present randomized clinical trial, a calculation has been made based on the detection of significant differences in two main variables:

1. Muscle mass, evaluated by Vector Bioimpedance (BIVA).
2. Muscle strength, measured through hand-grip dynamometry.

Statistical parameters used

The following values, obtained from previous reviews on β-hydroxy-β-methylbutyrate (HMB) supplementation in patients with chronic diseases and cancer, have been considered:

- For muscle mass (BIVA):
    - Minimum relevant difference (Δ\DeltaΔ): 0.8 kg.
    - Standard deviation (σ\sigmaσ): 1.2 kg.
- For muscle strength (grip dynamometry):
    - Minimum relevant difference (Δ\DeltaΔ): 2.0 kg.
    - Standard deviation (σ\sigmaσ): 3.5 kg.
- Other statistical considerations:
    - Significance level (α\alphaα): 0.05 (5%).
    - Statistical power (1−β1-\beta1−β): 0.80 (80%).

Sample size calculation

To compare two independent means between the control group (without HMB) and the experimental group (with HMB), the formula for Student's t-test for independent samples has been used:

$$n = \frac{(Z_{\alpha/2} + Z_{\beta})^2 \cdot 2\sigma^2}{\Delta^2}$$

Where:

- Zα/2=1.96Z = 1.96Zα/2=1.96 for a 95% confidence level.

- Zβ=0.84Z=0.84Zβ=0.84 for 80% power.

Since the most demanding estimate comes from the analysis of muscle strength, the sample size necessary to ensure sufficient power in both variables is 49 participants per group (98 in total).

To compensate for possible losses during follow-up (an additional 20%), the recommended recruitment size is 118 participants in total.

The sample size is divided into two parallel groups of equal size:

- Experimental Group (49 patients): Will receive the protein module (ProSup Protein®; Persan Farma S.L.) (Annex I) at the recommended dose according to the patient's protein needs.
- Comparison Group (49 patients): You will receive standard treatment, ensuring that your nutritional needs are met.

This sample size allows us to evaluate the feasibility of the protocol and to explore relevant clinical differences between groups with greater statistical confidence than a smaller design.
In the comparison group, all patients will receive standard nutritional treatment derived from routine clinical practice, ensuring that the patient's nutritional needs are met. This addresses potential ethical concerns related to lack of treatment in the control group, ensuring a safe and clinically appropriate approach for all participants.

Variables

Exposure Variables

1. **Type of Nutritional Intervention**:
    - Experimental Group: Nutritional and physical exercise program + Protein module enriched with HMB (*ProSup Protein®*).
    - Comparative Group: Nutritional and physical exercise program of routine clinical practice.

Descriptive Variables

Sociodemographic (age, sex), Anthropometric (usual weight, current weight, BMI), clinical (type of pathology, comorbidities), dietary intake (dietary record 72H previous IENVA)

Effect or Outcome Variables

Primaries

1. **Change in physical functionality:**
    - **Description**:

1. Hand/quadriceps dynamometry (kg)
2. Squats (5 STS, sec; nº squats/30 sec)
3. Test Timed Up and Go. Score in seconds.
4. 20 RM (kg)

- Time of evaluation: Baseline, 3 months.

2. **Body composition:**
    - **Description:**
        1. Area (cm2), anteroposterior axis (y-axis, cm) (in relaxation and contraction) of the anterior rectus quadriceps muscle by nutritional ultrasound.
        2. Electrical parameters of BIVA (Body Cell Mass (kg), Phase Angle (PA, º), Standardized Phase angle (SPa, º), Nutrigram, Hidragram.
        3. BIVA muscle parameters (Fat Free Mass Indedx (FFMI), Appendicular Skeletal Mass Index (ASMI), Skeletal Mass Index (SMI), kg/m2).
    - **Measurement time:** Baseline, 3 months.
3. Nutritional parameters:
    - **Description:**
        1. GLIM criteria for the diagnosis of disease-related malnutrition (ANNEX II)
        2. EWGSOP2 criteria for the diagnosis of sarcopenia (ANNEX III)

Secondary

1. **Adherence to the module:**
    - **Description:** Adherence record by means of a questionnaire (Wanden-Berghen Scale) and quantitative analysis of the actual intake of the protein module
    - **Measurement time:** 1.5 months, 3 months.

2. **Tolerance:**
    - **Description**: Record of adverse effects derived from the intake of the protein module.
    - **Time of evaluation**: 1.5 months, 3 months.

Data collection strategy

1. **Scheduled Visits:**
    - Data will be collected at 3 visits: baseline and 1.5 months (telephone), 3 months final follow-up visit.
    - Each face-to-face visit will include the measurements of the variables under study according to the planned schedule.
2. **Training of Evaluators:**
    - All personnel in charge of data collection are trained in the use of validated instruments and tools, as well as in the uniformity of the protocol.
3. **Data Management and Validation REVIEW ROCÍO**
    1. **Encoding and Storage:**
        - The data collected will be entered into a data collection notebook (Excel), designed specifically for this study.
        - Each participant will be identified by a unique code, guaranteeing anonymization.
    2. **Audits and Monitoring:**
        - Data quality monitoring will be done on a regular basis to identify inconsistencies or outliers.
    3. **Data Protection:**
        - The data will be stored on secure servers, with restricted access to the research team.
        - It will comply with current regulations on the protection of personal data (LOPD-GDD and GDPR).

Data management

Data Collection

- Data will be collected during scheduled visits (baseline, 1.5 months and 3 months) by trained professionals.
- The measurements will be entered directly into a Data Collection Notebook (Excel) designed specifically for this study, following the established protocol.

Coding

- Each participant will be identified by a unique alphanumeric code, guaranteeing anonymity.
- Directly identifiable information such as names or personal identification numbers will not be stored in conjunction with clinical or laboratory data.
- The database will include coded and validated variables to facilitate statistical analysis, while maintaining the integrity of the information.

Storage

- The data collected will be stored on secure servers with restricted access, managed by a clinical data management system (CDMS) in accordance with international security standards.
- Backups will be made periodically to prevent loss of information and ensure the continuity of the study.

Processing

- The data will be reviewed and validated by an independent monitoring team before proceeding to statistical analysis.
- Inconsistencies, outliers, or missing data will be reviewed and fixed through consultation with the responsible centers.
- The management system will include regular audits to ensure the quality and consistency of the data entered.

Data Protection

- The data will be handled in compliance with current personal data protection regulations (LOPD-GDD and GDPR).
- All personnel involved will sign confidentiality agreements and be trained in the secure handling of information.

Access and Monitoring

- Access to Excel and CRD on paper will be restricted to principal investigators and the authorized data management team only.
- The participating centre will have access only to the data corresponding to its own patients, ensuring inter-institutional confidentiality.

Anonymization for Analytics

- Prior to analysis, the data will be anonymized by removing any information that allows the identification of participants.

- The unique code assigned to each patient will be used exclusively during the statistical analysis and will be decoupled from the identifying information at the end of the study.

Data Retention and Deletion

- The anonymised data will be retained for a period of 5 years after the publication of the results, as stipulated in the international regulations for clinical research.
- Subsequently, the data will be securely deleted using certified procedures.

Data analysis

The analysis of the data will be carried out using advanced statistical tools to respond to the objectives of the study and test the hypothesis raised. Jamovi statistical software will be used to perform the descriptive, inferential and multivariate analyses. The statistical methods that will be used are detailed below:

For quantitative variables, descriptive measures such as means, standard deviations, and ranges will be calculated; categorical variables will be described using frequencies and percentages. Baseline comparability of groups will be assessed using Student's t-test or Mann-Whitney U test for continuous variables, and Chi-square or Fisher's exact tests for categorical variables. Intra- and intergroup changes over time (baseline, 1.5 months, and 3 months) will be analyzed with an ANOVA for Repeated Measures (ANOVA-RM) or equivalent nonparametric tests such as Friedman's.

Multivariate analyses, such as linear and logistic regressions, will be used to identify predictors of change in primary variables.

The significance level will be $p < 0.05$, applying Bonferroni correction for multiple tests. The results will be presented in graphs and tables that reflect changes in nutritional, functional, and inflammatory parameters over time. In addition, an intention-to-treat (ITT) and per-protocol (PP) analysis will be performed to ensure the robustness of the findings.

Quality Control

The study will be conducted in compliance with local laws and regulations. Approval by the competent CEIm (Malaga Provincial Ethics Committee) will be carried out as required in accordance with local laws and regulations. The patient's authorization to use and/or disclose his/her anonymized health data will be obtained prior to the patient's inclusion through informed consent.

To maintain the confidentiality of the subjects, no demographic data that can identify the patient will be collected. Only the data specified in the research plan will be sent for biostatistical analysis.

Limitations of research methods

The present pilot study, although designed to explore the efficacy and tolerance of an HMB-enriched protein module in patients with increased protein requirements, has some inherent limitations to its design that may influence the generalizability and external validity of the results.

1. **Duration of the Study:**
    - The 3-month follow-up may not capture the long-term effects of the module on body composition. Longer studies would be needed to confirm the sustainability of the results.
2. **Uncontrolled Confusion Effects:**
    - Although it will be adjusted for factors such as age, sex, and comorbidities, it is possible that other factors, such as variations in usual diet or physical activity outside the protocol, may influence the results.

Despite these limitations, the design of this pilot study allows to evaluate the feasibility of the protocol and estimate key parameters, thus improving the evidence base for the implementation of individualized nutritional interventions.

PROTECTION OF THE PERSONS SUBJECT TO THE STUDY

Ethical and legal aspects:

This study will be carried out in compliance with the basic ethical principles and standards that have their origin in the current revision (revised version of Fortaleza, 2013) of the Declaration of Helsinki approved by the World Medical Assembly, the Oviedo Convention, and with the current regulatory requirements set out in Royal Decree 957/2020, of 3 November, which regulates observational studies with medicinal products for human use.
The study will be conducted in compliance with the provisions of this protocol. Before starting the study, the Drug Research Ethics Committee (CEIm) must approve or give its favorable opinion to the protocol and all its amendments. The rights, safety, and well-being of the patients in the study are the most important considerations to take into account and should prevail over the interests of science and society.

Likewise, this study will be in accordance with the specific regulations of the Autonomous Communities where it is carried out. The development of the study will not interfere with the doctor's prescribing habits. Suspected adverse reactions will be recorded and notified in accordance with current legislation and good pharmacovigilance practices.

Informed consent:

In patients who are included in the study after the date of approval of the study, informed consent will be requested. For the request for informed consent, the ethical rules and principles relating to the provisions in relation to the collection, storage and possible future use of the subjects' biological samples will be taken into account.

Protection of personal data:

The collection of personal and clinical data is exclusively for the purpose of fulfilling the objectives of the study.

The collection, processing and analysis of the data will be carried out in accordance with the General Data Protection Regulation 2016/679 of December and Organic Law 03/2018 of 5 December on the protection of personal data and guarantee of digital rights and Law 41/2002, of 14 November, basic regulation of patient autonomy and rights and obligations in terms of clinical information and documentation.

The data collected for these studies will be collected in:

- a data collection notebook (paper)
- An electronic data collection notebook

- The data will be entered into a database identified only by means of a code, so no information will be included that allows the identification of the participants. Only the study investigator and his collaborators with the right of access to the source data (medical history) will be able to relate the data collected in the study with the patient's medical history.

The identity of the participants will not be available to any other person except for a medical emergency or legal requirement.

The health authorities, the Ethics Committee for Research with Medicines and the personnel authorized by the sponsor of the study may have access to the personally identified information, when necessary to verify data and procedures of the study, always maintaining confidentiality in accordance with current legislation.

Data processing:

As promoters of the project, we are committed to processing the data in accordance with EU Regulation 2016/679 and, therefore, to keep a record of the processing activities we carry out and to carry out a risk assessment of the processing we carry out, to know what measures we will have to apply and how to do it.

In addition to the rights of access, modification, opposition and deletion of data, participants may limit the processing of data collected for the project that is incorrect, request a copy or that it is transferred to a third party. To exercise these rights, they must contact the principal investigator of the study. They also have the right to contact the Data Protection Agency if they are not satisfied. The data cannot be deleted, even if a patient leaves the study, to ensure the validity of the research and to comply with legal duties and drug authorization requirements.
Researchers will keep the essential documentation and materials of the study for at least 5 years after the end of the study or for a longer period if other legal requirements so provide.

MANAGEMENT AND NOTIFICATION OF ADVERSE REACTIONS AND OTHER RELEVANT EVENTS THAT APPEAR DURING THE STUDY:

Suspected adverse reactions detected in the course of the study will be reported within fifteen calendar days of the date of receipt, for severe cases, and within ninety calendar days of receipt for non-serious cases. This notification will be made through the electronic form provided by the AEMPS www.notificaram.es.

WORK PLAN (TASKS, MILESTONES AND CHRONOLOGY OF THE STUDY)

Starting point for planning the project activities. In this section, the activities necessary to complete the study must be defined.

The study will be carried out during the 12 months following the approval of this protocol, during which time the data collection and subsequent statistical analysis are established. The expected duration of the recruitment period is 6 months.

The stages of the study will be distributed as follows:

STAGES	PERIOD
CEIm Approval	March-April 2025
Foundation Contract	April 2025
Start of recruitment	May- June 2025
End of recruitment	November-December 2025
Analysis of the results	February 2026
Final report of the results of the study	April 2026
Dissemination of results	May 2026--

PLANS FOR DISSEMINATION AND COMMUNICATION OF THE RESULTS OF THE STUDY

The sponsor undertakes to make public the results of the study, both positive and negative.

The results will be presented at national and international conferences and published in peer-reviewed scientific journals to ensure their wide dissemination and impact in the scientific and medical community.

4. Bibliography

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ANNEX I: ProSup Protein® Fact Sheet

ProSUP PROTEIN

CODE 110000940

DESCRIPTION

Food for special medical purposes.

Whey protein module enriched with HMB.

For the dietary management of patients with deficient protein intake or increased protein requirements.

Presentation	Flavour	C.I.	Type	Subtype
Box containing 30 sachets of 12.4 g	Neutral	505607	MPEN	MPEN1

CHARACTERISTICS

Caloric density:	0.22 kcal/ml
Energy distribution:	P / CH / F / E: 89.2 / 9.5 / 1.3 / 0
Osmolarity:	81 mOsm/l
Non-protein kcal/g N:	3.0

	per 100 g	Per sachet (12.4 g)	per 100 ml solution	% Energy value
Energy value (kJ)	1523	189	10	
Energy value (kcal)	359	44	2	
Fat (g)	0.5	0.1	0	1.3
of which: saturates (g)	0.3	0	0	
Carbohydrate (g)	8.5	1.1	0.5	9.5
of which:				
sugars (g)	0.45	0.06	0.03	
lactose (g)	0.45	0.06	0.03	
Protein (g)	80	10	4.9	89.2
Salt (g)	0.45	0.06	0	
of which: sodium (mg)	179	22	11	

***One 12.4 g sachet dissolved in 200 ml of water is equivalent to 202 ml of standard solution**

COMPOSITION

Minerals	per 100 g	Per sachet (12.4 g)	per 100 ml solution
Whey protein isolate (WPI) (g)	80	10	4.9
HMB-Ca (g)	11	1.3	0.66
HMB (g)	8.1	1.0	0.49

ORGANOLEPTIC CHARACTERISTICS

Appearance	Appearance in solution	Color	Odor and taste
Fine powder	Translucent white	White	Neutral, slightly milky

ANNEX II:

GLIM Criteria (Global Leadership Initiative on malnutrition).

Malnutrition requires at least 1 phenotypic criterion and 1 etiologic criterion:

PHENOTYPIC CRITERIA			ETIOLOGIC CRITERIA	
Unintentional weight loss	**Low body mass index (kg/m²)**	**Reduced muscle mass**	**Reduced food intake or assimilation**	**Inflammatory burden**
> 5% in the last 6 months or > 10% in more than 6 months	<20 if <70 y or <22 if >70 y	Using validated body composition techniques	? 50% >1 wk, or ? 100% >2 wk, or any chronic gastrointestinal condition that alters food assimilation	Acute injury/ inflammation. Chronic inflammatory disease.

ANNEX III:

Operational definition of sarcopenia

Probable sarcopenia is identified using Criterion 1.

The diagnosis is confirmed by additional Criterion 2 documentation.

If criteria 1, 2, and 3 are met, sarcopenia is considered severe.

1. Low muscle strength (**dynapenia**)
2. Low muscle quantity or quality or **pre-sarcopenia** (low asthma or SIM)
3. **Confirmed sarcopenia** : dynapenia + pre-sarcopenia together
4. **Severe Sarcopenia:** Sarcopenia + Poor Physical Performance (tug >20)

Sarcopenia cut-off points EWGSOP2

Test	**Cut-off points for men**	**Cut-off points for women**
EWGSOP2 sarcopenia cut-off points for low strength using chair rise and handgrip strength		
Handgrip strength	**<27 kg**	**<16 kg**
Chair rise	**>15 s for five rises**	
EWGSOP2 sarcopenia cut-off points for low muscle quantity		
ASM	**<20 kg**	**<15 kg**
ASM/height²	**<7.0 kg/m²**	**<5.5 kg/m²**
EWGSOP2 sarcopenia cut-off points for low physical performance		
Gait speed	**<=0.8 m/s**	
SPPB	**<=8 points**	
TUG	**>=20 s**	
400 m walk test	**Does not complete or >=6 min to complete**	

Abbreviations:

ANNEX IV

Dimension	Items	Response (score)	
Knowledge	C1 Do you know why you are taking nutrition?	Yes (1)	No (0)
	C2 Do you know the trade name of the nutrition you are given?	Yes (1)	No (0)
	C3 Do you think you know how nutrition should be taken?	Yes (1)	No (0)
Dimension Score		Classification	
0		Ignorant	
1-2		Average connoisseur	
3		Good connoisseur	
Difficulties	D1 Have you ever had to stop taking or taking nutrition?	Yes (1)	No (0)
	D2 Did the amount you have been told ever vary?	Yes (1)	No (0)
	D3 Do you change the timing of the feedings for any reason?	Yes (1)	No (0)
Dimension Score		Classification	
0		Poor compliance	
1-2		Average Compliant	
3		Good compliance	
Total score of the two dimensions		Sum of the dimensions	Classification
		0-2	Low
		3-4	Media
		5-6	High

Table 9. Adherence questionnaire. Wanden-Berghe C, Cheikh Moussa K, Sanz-Valero J. Adherence to Home Enteral Nutrition. Hosp Domic. 2018; 2(1):11-8