UNIVERSITÀ DEGLI STUDI DI MILANO

CORSO DI DOTTORATO IN SCIENZE DELLA NUTRIZIONE
XXXII CICLO

DIPARTIMENTO DI
SCIENZE CLINICHE E DI COMUNITA'

TESI DI DOTTORATO DI RICERCA:

MALNUTRITION AND PHYSICAL PERFORMANCE IN NURSING HOME RESIDENTS: RESULTS FROM THE INCUR STUDY

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A.A. 2019/2020

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i miei piccoli e preziosi aiutanti

INDEX

ABSTRACT

Objectives: to investigate the association between malnutrition and physical performance in nursing home residents.

Design: cross sectional study.

Setting and Participants: a total of 499 older people (73.1% women) enrolled in the Incidence of pNeumonia and related ConseqUences in nursing home Residents (INCUR) cohort study.

Methods: the nutritional status was defined using the Mini Nutritional Assessment–Short Form (MNA-SF), whereas the physical performance was measured with the Short Physical Performance Battery (SPPB). Unadjusted and adjusted (for age, sex, education, Abbreviated Mental Test score and Charlson Comorbidy Index) linear regression analyses were used to assess the association between MNA-SF and SPPB (primary outcome). The MNA-SF items which seemed most strongly related to the SPPB (and its subtasks) were also explored. Finally, we explored the association of the MNA-SF with each subtest of the SPPB.

Results: the mean age of the sample was 85.80 (standard deviation, SD 7.20). The mean SPPB score was 3.05 (SD 2.65) and the mean MNA-SF score 10.35 (SD 2.22). Higher scores of MNA-SF were associated with better physical performance. Food intake deficiency, mobility impairment, and recent psychological stress or acute disease were the items of the MNA-SF most strongly associated with the SPPB, even after adjustment for potential confounders. Among the three subtests of the SPPB, the MNA-SF showed the strongest and most consistent association with the gait speed.

Conclusions and Implications: among nursing home residents, the MNA-SF and three of its sub-items (food intake deficiency, mobility impairment, and recent psychological stress) are significantly correlated with physical performance, independently of potential confounders. In particular, the association was evident for the gait speed subtask of the SPPB.

INTRODUCTION

Malnutrition

Malnutrition can be defined as a state resulting from lack of uptake or intake of nutritional elements leading to altered body composition and body cell mass[1]. Its causes are heterogeneous: starvation[2], cachexia[3] or simply aging[4].

Malnutrition diminishes physical and mental functions predisposing to the development of adverse clinical outcomes from diseases[1]. Moreover, it increases the risk of hospitalization and mortality[5-8].

Though the above-mentioned definition is well accepted, no univocal diagnostic criteria for malnutrition exist. The clinical characteristics used to define malnutrition have varied over time combining many clinical, anthropometrical, and biochemical measures[9,10].

Clinical indicators of malnutrition

The clinical manifestations of nutrition deficiencies can be used to identify some cases of malnutrition. Unfortunately, signs and symptoms of micronutrient deficiencies tend to appear only when the deficit is severe. Moreover, confounding factors leading to similar manifestations, should be taken into account. *Table 1* illustrates the clinical indicators of some micronutrient deficiencies.

Table 1: clinical indicators of some micronutrient deficiencies

Clinical indicator	Micronutrient deficiency
Pallor of palms or inside of eyelids or mouth	Iron deficiency anaemia
Night blindness	Vitamin A deficiency
Bitot's spots	Vitamin A deficiency
Goitre	Iodine deficiency

Anthropometrical measures of malnutrition

The main anthropometrical measures used to identify malnutrition are body mass index (BMI) and calf circumference (CC).

BMI has been used to assess the degree of the body thinness . BMI is calculated as the body weight (in kg) divided by the square of the height (in meters).

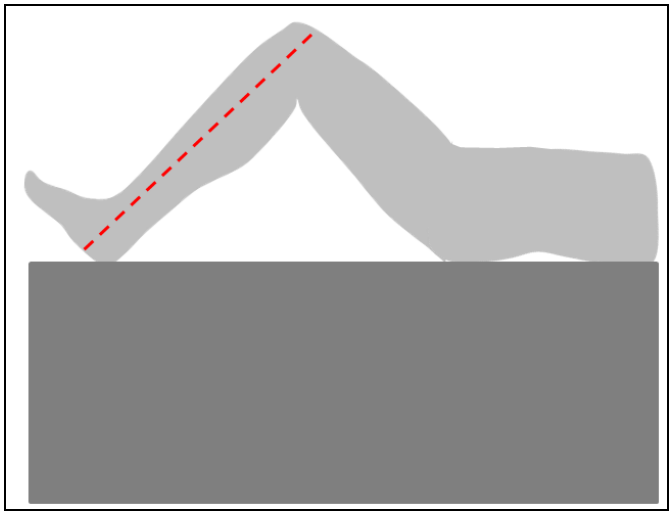
If the patient cannot stand upright or has a spine curvature problem, the height can be derived by using other anthropometric measures through ad hoc formulas.

The Chumlea formula (*Table 2*) estimates the height from the heel-knee length. The knee length is measured with the patient lying on his back and knees bent at 90° (*Figure 1*)[11].

Table 2: Chumlea formula

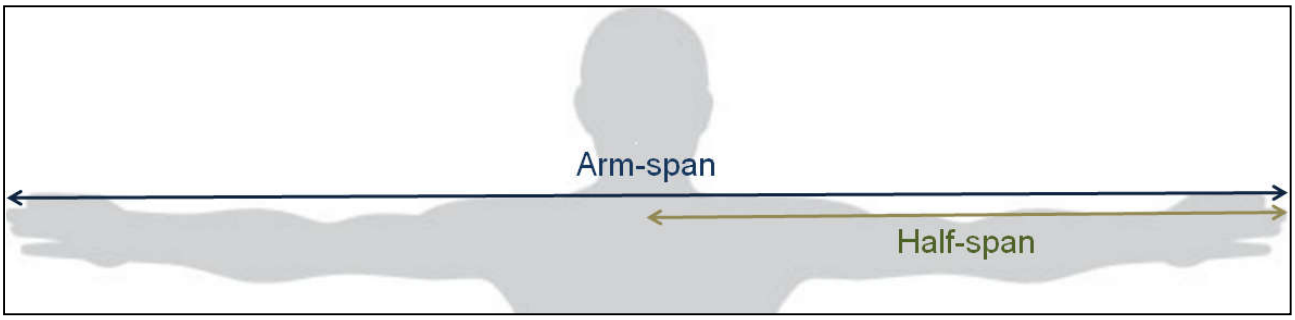
Chumlea formula	
Women	H (cm) = 84.88 - 0.24 x age (years) + 1.83 x knee height (cm)
Men	H (cm) = 64.19 - 0.04 x age (years) + 2.03 x knee height (cm)

Figure 1: measurement of the heel-knee length



Another anthropometric measure used to derive the height is the half arm span (*Figure 2*). It is the distance from the middle of the sternal notch to the tip of the middle finger. It is measured with the arm held out horizontally to the side. Both sides should be measured. If there is a discrepancy, the measurements should be repeated and the longest one taken.

Figure 2: Measurement of the half arm span.



The Height is derived from the following formula.

Height (cm) = [0.73*(2 *half arm span (cm))] + 0.43

According to the World Health Organization (WHO) a BMI < 18.5 kg/m^2 is consistent with a state of malnutrition[12].

Table 3 illustrates the classification of malnutrition in adults according to BMI categories.

Table 3: classification of malnutrition in adults by BMI

BMI (kg/m^2)	Nutritional status
≥ 18.5	Normal
17-18.49	Mild malnutrition
16-16.99	Moderate malnutrition
< 16	Severe malnutrition

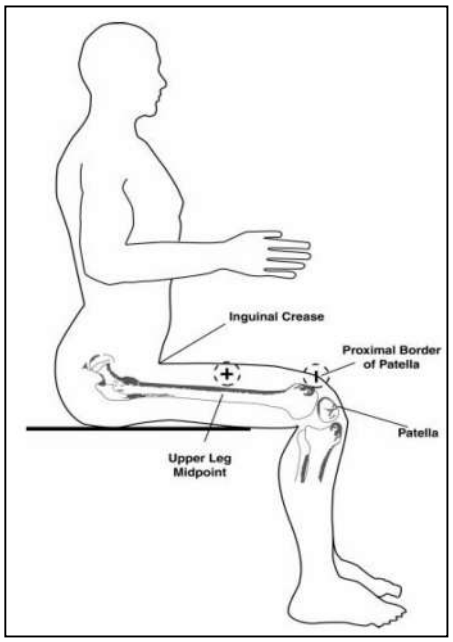
Even if these cut-offs are useful for public health studies[13], their clinical relevance may be questioned. Indeed, the escalating global epidemic of overweight and obesity cannot be taken into account. Overweight and obese people may suffer from malnutrition in spite of having BMI values ≥ 18.5 kg/m^2.

Moreover, since in older people higher BMI have been associated with a better survival, different cut off points have been proposed. Lipschitz suggested a value of BMI of 22 kg/m^2 to define malnutrition in older people[14] whereas the European Society of Clinical Nutrition and Metabolism (ESPEN)[15] proposed to use a cut point of 20 kg/m^2 in people < 70 years and of 22 kg/m^2 in people above 70.

The CC can be useful to estimate the lean mass[16]. It was first validated as a screening tool for reduced muscle mass by Rolland[17]. Rolland validated a cut-off point of 31 cm as a threshold of reduced muscle mass. A reduced CC was associated to difficulties in performing daily living activities (lifting and reaching objects, walking, going upstairs or downstairs, standing up from a chair and rising from bed).

The maximal CC should be measured by putting the patient in a sitting position with the knee and ankle at a right angle and feet resting on the floor. There is not a unique consensus on which leg should be used for the assessment[18,19]. The measuring tape should be placed around the calf and moved up and down to locate the maximum circumference in a plane perpendicular to the long axis of the calf (*Figure 3*). Subcutaneous tissues should not be compressed.

Figure 3: Measurement of calf circumference



Biochemical markers of malnutrition

Laboratory markers have a complementary role to the physical examination in the diagnosis of malnutrition. They cannot be used alone since their specificity is low. Indeed, their levels are influenced both by inflammatory statuses and diseases (renal or hepatic failure, enteropathies, over-hydration)[20]. Inflammatory signals (like IL-6 and TNF-alpha) are potent inhibitors of visceral protein synthesis[21]; moreover, they can cause nutritional protein degradation.

The main visceral proteins used as malnutrition biomarkers are albumin and prealbumin. Nowadays prealbumin is often preferred to albumin due to its shorter half live (2-3 days versus 10), thus reflecting more rapid changes of the nutritional status[9].

The role of transferrin as a nutritional biomarker is debated[22-24]. Even if its levels decrease in case of severe malnutrition, they are an unreliable marker of mild malnutrition[25]. This is because transferrin concentration is influenced by iron status (it increases in case of iron deficiency) and

renal disease and inflammatory status (increased levels). Moreover, it has a relative long half-life (about 10 days) and like albumin it cannot reproduce acute changes of nutritional status.
Low serum cholesterol concentrations have been associated with an increased mortality[26]. However, cholesterol is neither sensitive nor specific to monitor malnutrition.

Malnutrition has been associated to an altered maturation of lymphocytes. Therefore, a reduced lymphocytes count (< 1500/ mm^3) has been proposed as a marker of malnutrition[27]. Anyway, this parameter is influenced by both intercurrent diseases and severe stresses.

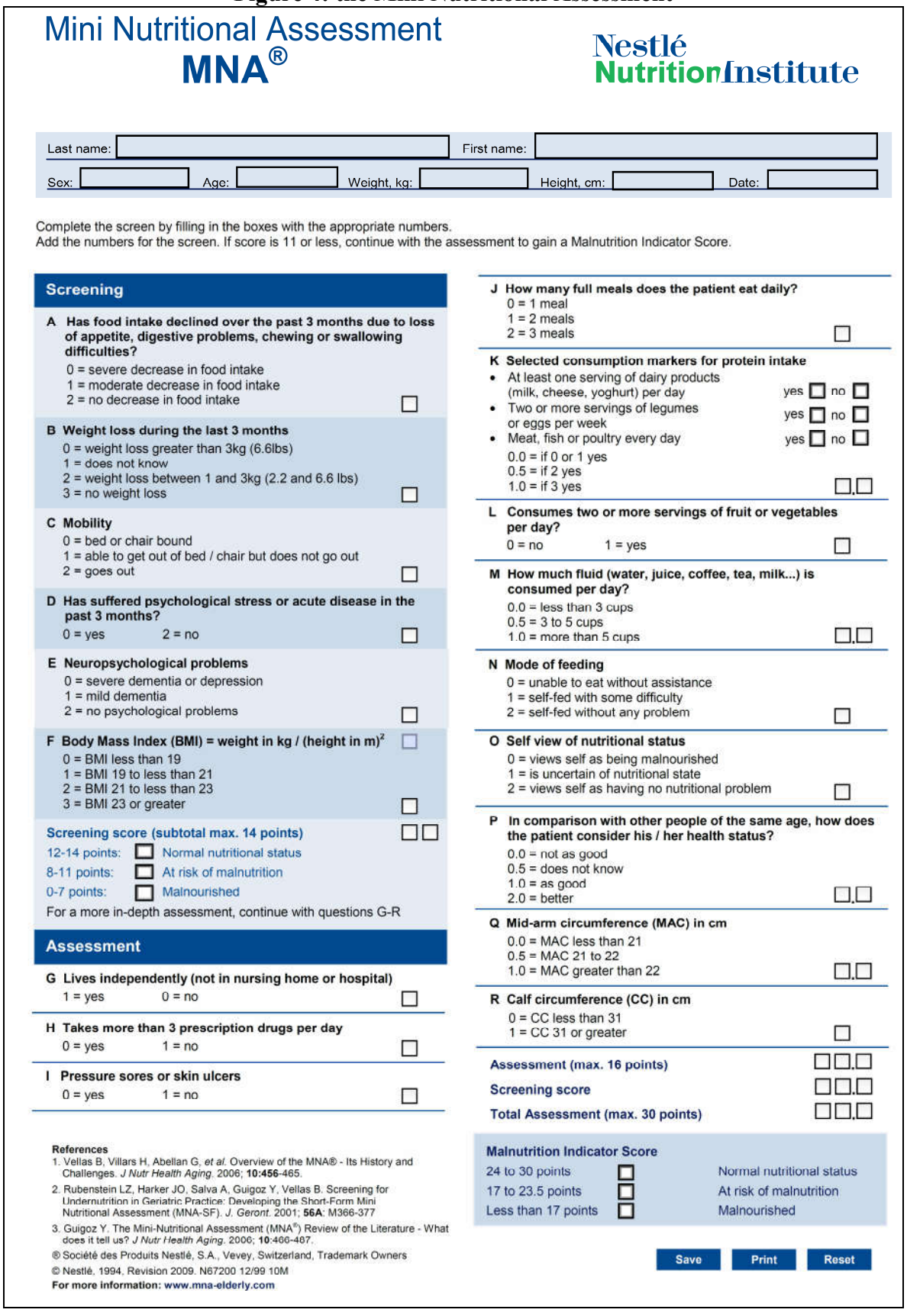
Mini nutritional assessment: a screening tool for malnutrition

The Mini Nutritional Assessment (MNA) is a screening tool for malnutrition[28] (*Figure 4*), specifically designed to early detect nutritional problems in older adults.
It is composed by 18 items (with a total score of 30 points) covering anthropometric, general, dietary and subjective aspects. The thresholds to define malnutrition (a score < 17) and risk of malnutrition (a score between 17 and 23.5) have been clearly defined.
It has been validated in many studies[28] and demonstrated to be highly sensitive (96%), specific (98%), and reproducible. Moreover, it is easily usable by generalist assessors with a minimal risk of bias introduction by the data collector. It is accepted by patients and can be also administered in people suffering from cognitive impairment (with the help of caregivers) and in immobile individuals. Finally, it is inexpensive and even adapt to resource-poor settings.
The administration of MNA involves two-steps: a nutritional screening composed by the first six items of the full MNA and then, just for people resulting at risk of malnutrition (a score ≤ 11), the complete test.
The screening is also known as MNA short form (MNA-SF)[29]. It has a total score of 14 points and requires less than 5 minutes to be performed. It has a strong correlation with the full MNA[29,30] but it

has also been validated as an independent tool for nutritional screening in older adults[31]. Indeed, it proved to accurately identify individuals at risk of malnutrition (a score ≤ 11) or malnourished (a score ≤ 7) among nursing home residents[5,29,30].

Moreover, the MNA-SF with its 6 items which comprise both nutritional criteria (BMI, food intake and weight loss) and criteria related to "geriatric conditions" (mobility, recent acute stress and neuropsychological disorders) can provide insights into the global health apart from the mere nutritional status. Therefore, the MNA-SF can be considered a multidimensional instrument able to capture the risk profile of individuals who are exposed to negative events (i.e. reduced physical performance and risk of disability) and can be used as a potential frailty instrument in older people.

Figure 4: the Mini Nutritional Assessment



Mini Nutritional Assessment
MNA®

Nestlé Nutrition Institute

Last name: First name:

Sex: Age: Weight, kg: Height, cm: Date:

Complete the screen by filling in the boxes with the appropriate numbers.
Add the numbers for the screen. If score is 11 or less, continue with the assessment to gain a Malnutrition Indicator Score.

Screening

A Has food intake declined over the past 3 months due to loss of appetite, digestive problems, chewing or swallowing difficulties?
0 = severe decrease in food intake
1 = moderate decrease in food intake
2 = no decrease in food intake

B Weight loss during the last 3 months
0 = weight loss greater than 3kg (6.6lbs)
1 = does not know
2 = weight loss between 1 and 3kg (2.2 and 6.6 lbs)
3 = no weight loss

C Mobility
0 = bed or chair bound
1 = able to get out of bed / chair but does not go out
2 = goes out

D Has suffered psychological stress or acute disease in the past 3 months?
0 = yes 2 = no

E Neuropsychological problems
0 = severe dementia or depression
1 = mild dementia
2 = no psychological problems

F Body Mass Index (BMI) = weight in kg / (height in m)²
0 = BMI less than 19
1 = BMI 19 to less than 21
2 = BMI 21 to less than 23
3 = BMI 23 or greater

Screening score (subtotal max. 14 points)
12-14 points: Normal nutritional status
8-11 points: At risk of malnutrition
0-7 points: Malnourished
For a more in-depth assessment, continue with questions G-R

Assessment

G Lives independently (not in nursing home or hospital)
1 = yes 0 = no

H Takes more than 3 prescription drugs per day
0 = yes 1 = no

I Pressure sores or skin ulcers
0 = yes 1 = no

J How many full meals does the patient eat daily?
0 = 1 meal
1 = 2 meals
2 = 3 meals

K Selected consumption markers for protein intake
- At least one serving of dairy products (milk, cheese, yoghurt) per day yes no
- Two or more servings of legumes or eggs per week yes no
- Meat, fish or poultry every day yes no

0.0 = if 0 or 1 yes
0.5 = if 2 yes
1.0 = if 3 yes

L Consumes two or more servings of fruit or vegetables per day?
0 = no 1 = yes

M How much fluid (water, juice, coffee, tea, milk...) is consumed per day?
0.0 = less than 3 cups
0.5 = 3 to 5 cups
1.0 = more than 5 cups

N Mode of feeding
0 = unable to eat without assistance
1 = self-fed with some difficulty
2 = self-fed without any problem

O Self view of nutritional status
0 = views self as being malnourished
1 = is uncertain of nutritional state
2 = views self as having no nutritional problem

P In comparison with other people of the same age, how does the patient consider his / her health status?
0.0 = not as good
0.5 = does not know
1.0 = as good
2.0 = better

Q Mid-arm circumference (MAC) in cm
0.0 = MAC less than 21
0.5 = MAC 21 to 22
1.0 = MAC greater than 22

R Calf circumference (CC) in cm
0 = CC less than 31
1 = CC 31 or greater

Assessment (max. 16 points)
Screening score
Total Assessment (max. 30 points)

Malnutrition Indicator Score
24 to 30 points: Normal nutritional status
17 to 23.5 points: At risk of malnutrition
Less than 17 points: Malnourished

Save Print Reset

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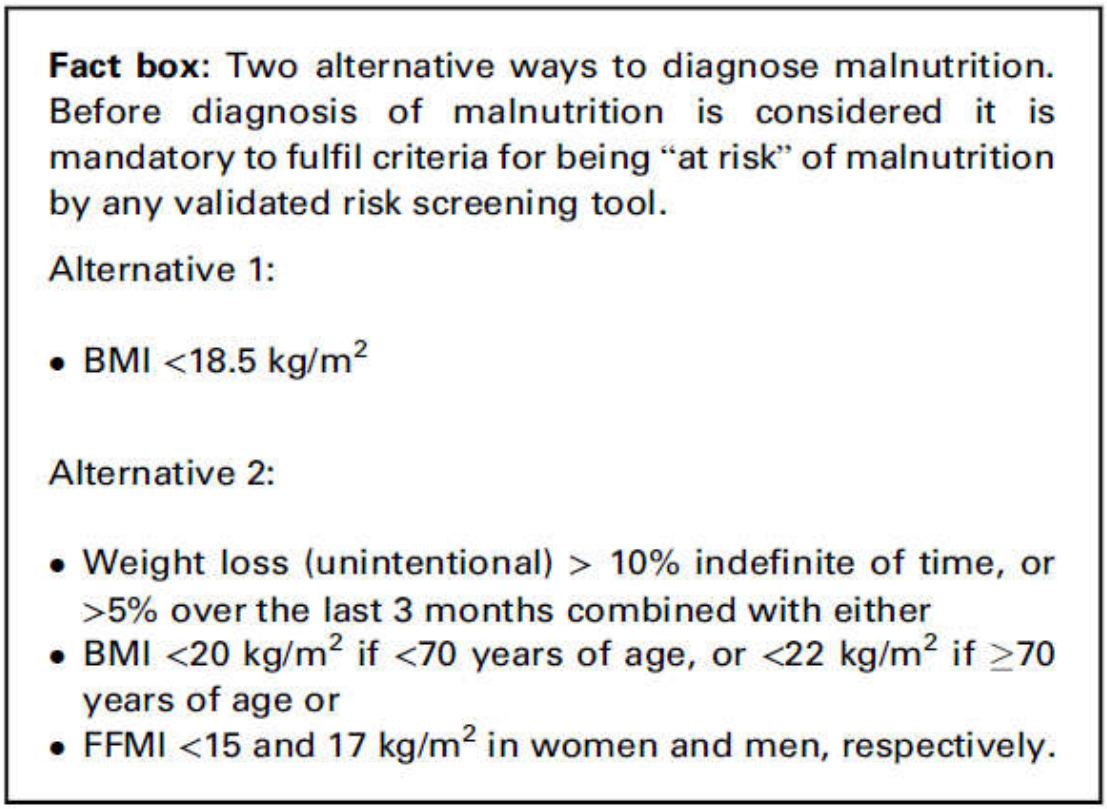
For more information: www.mna-elderly.com

Diagnostic criteria for malnutrition

European Society of Clinical Nutrition and Metabolism criteria

In 2015 the European Society of Clinical Nutrition and Metabolism (ESPEN) validated updated diagnostic criteria for malnutrition[15]. The diagnosis of malnutrition could be performed if BMI was <18.5 kg/m^2 or if an unintentional weight loss was associated to either a reduced BMI (<20 kg/m^2 in people < 70 years or <22 kg/m^2 in people ≥ 70 years) or a low-fat free mass index. Moreover, ESPEN recommends to screen for malnutrition all individuals who are potentially at risk (*Figure 5*).

Figure 5: ESPEN criteria for malnutrition diagnosis



The Global Leadership Initiative on Malnutrition criteria

The Global Leadership Initiative on Malnutrition (GLIM) is an initiative focused on building a global consensus around core diagnostic criteria for malnutrition in adults. It was endorsed by the

major global clinical nutrition societies: the American Society for Parenteral and Enteral Nutrition (ASPEN), ESPEN, the Federatiòn Latino-Americana de terapia nutricional, nutriciòn clinica y metabolismo (FELANPE), and The Parenteral and Enteral Nutrition Society of Asia (PENSA). The developed consensus criteria were thought to be suitable to diverse clinical settings[32].

Moreover, the work underlined the importance of screening all at risk individuals with adequate tools. Five criteria for defining malnutrition were then identified: weight loss, low BMI, reduced muscle mass (phenotypic criteria), reduced food intake or assimilation and disease burden/inflammation (etiologic criteria). The diagnosis requires the presence of at least one phenotypic and one etiologic criterion (*Table 4*).

Table 4 phenotypic and etiologic criteria for the diagnosis of malnutrition

Phenotypic Criteria*			Etiologic Criteria*	
Weight loss (%)	Low body mass index (kg/m^2)	Reduced muscle mass[a]	Reduced food intake or assimilation[b, c]	Inflammation[d,e,f]
>5% within past 6 months, or>10% beyond 6 months	<20 if <70 years, or <22 if >70 years Asia: <18.5 if <70 years, or <20 if >70 years	Reduced by validated body composition measuring techniques[a]	≤50% of ER >1 week, or any reduction for >2 weeks, or any chronic GI condition that adversely impacts food assimilation or absorption[b,c]	Acute disease/injury[d,f] or chronic disease-related[e,f]

*Requires at least 1 phenotypic criterion and 1 etiologic criterion for diagnosis of malnutrition.
[a]For example fat free mass index (FFMI, kg/m^2)) by dual-energy absorptiometry (DXA) or corresponding standards using other body composition methods like bioelectrical impedance analysis (BIA), CT or MRI. When not available or by regional preference, physical examination or standard anthropometric measures like mid-arm muscle or calf circumferences may be used. Thresholds for reduced muscle mass need to be adapted to race (Asia). Functional assessments like hand-grip strength may be considered as a supportive measure.
[b]Consider gastrointestinal symptoms as supportive indicators that can impair food intake or absorption e.g. dysphagia, nausea, vomiting, diarrhea, constipation or abdominal pain. Use clinical judgement to discern severity based upon the degree to which intake or absorption are impaired. Symptom intensity, frequency, and duration should be noted.
[c]Reduced assimilation of food/nutrients is associated with malabsorptive disorders like short bowel syndrome, pancreatic insufficiency and after bariatric surgery. It is also associated with disorders like esophageal strictures, gastroparesis, and intestinal pseudo-obstruction. Malabsorption is a clinical diagnosis manifest as chronic diarrhea or steatorrhea. Malabsorption in those with ostomies is evidenced by elevated volumes of output. Use clinical judgement or additional evaluation to discern severity based upon frequency, duration, and quantitation of fecal fat and/or volume of losses.
[d]Acute disease/injury-related. Severe inflammation is likely to be associated with major infection, burns, trauma or closed head injury. Other acute disease/injury-related conditions are likely to be associated with mild to moderate inflammation.
[e]Chronic disease-related. Severe inflammation is not generally associated with chronic disease conditions. Chronic or recurrent mild to moderate inflammation is likely to be associated with malignant disease, chronic obstructive pulmonary disease, congestive heart failure, chronic renal disease or any disease with chronic or recurrent Inflammation. Note that transient inflammation of a mild degree does not meet the threshold for this etiologic criterion.
[f]C-reactive protein may be used as a supportive laboratory measure.
GI = gastro-intestinal, ER = energy requirements

Table 5 describes the recommended thresholds for reduced muscle mass.

Table 5 examples of recommended thresholds for reduced muscle mass

	Males	Females
Appendicular Skeletal Muscle Index (ASMI, kg/m^2)[15]	<7.26	<5.25
ASMI, kg/m^2[2241]	<7	<6
ASMI, kg/m^2[2172]		
- DXA	<7	<5.4
- BIA	<7	<5.7
Fat free mass index (FFMI, kg/m^2)[8]	<17	<15
Appendicular lean mass (ALM, kg)[25]	<21.4	<14.1
Appendicular lean mass adjusted for BMI = ALM/BMI[26]	<0.725	<0.591

DXA = dual energy x-ray absorptiometry, BIA = bioelectrical impedance analysis
BMI = body mass index
[1]Recommendations from European Working Group on Sarcopenia in Older People 2 (EWGSOP2); personal communication Alfonso Cruz-Jentoft.
[2]Recommendations from Asian Working Group for Sarcopenia (AWGS) for Asians.

GLIM elaborated also criteria to grade the severity of malnutrition (*Table 6*).

Table 6: thresholds for severity grading of malnutrition

	Phenotypic Criteria[a]		
	Weight loss (%)	**Low body mass index (kg/m^2)[b]**	**Reduced muscle mass[c]**
Stage 1/Moderate Malnutrition (Requires 1 phenotypic criterion that meets this grade)	5–10% within the past 6 mo, or 10–20% beyond 6 mo	<20 if <70 yr, <22 if ≥70 yr	Mild to moderate deficit (per validated assessment methods – see below)
Stage 2/Severe Malnutrition (Requires 1 phenotypic criterion that meets this grade)	>10% within the past 6 mo, or >20% beyond 6 mo	<18.5 if <70 yr, <20 if ≥70 yr	Severe deficit (per validated assessment methods – see below)

[a]Severity grading is based upon the noted phenotypic criteria while the etiologic criteria described in the text and Figure 1 are used to provide the context to guide intervention and anticipated outcomes.
[b]Further research is needed to secure consensus reference BMI data for Asian populations in clinical settings.
[c]For example appendicular lean mass index (ALMI, kg/m^2) by dual-energy absorptiometry or corresponding standards using other body composition methods like bioelectrical impedance analysis (BIA), CT or MRI. When not available or by regional preference, physical examination or standard anthropometric measures like mid-arm muscle or calf circumferences may be used. Functional assessments like handgrip strength may be used as a supportive measure.[15]

Finally, an etiology-based diagnosis classification was proposed including four categories of malnutrition (*Table 7*).

Table 7: diagnosis category according to underlying etiology

Malnutrition related to
• Chronic disease with inflammation • Chronic disease with minimal or no perceived inflammation • Acute disease or injury with severe inflammation • Starvation including hunger/food shortage associated with socio-economic or environmental factors

Malnutrition in nursing homes

Malnutrition is a burdensome issue in the nursing home setting since it is highly prevalent and it is associated with many clinical adverse outcomes (mortality, hospitalizations, infections)[5,8,33].

The problem is amplified by the fact that the number of people living in nursing homes is in constant increase[34]. Indeed, recent literature identified malnutrition in istitutionalized people as an important and international research priority[35,36]. Unfortunately, research in this setting is scarce: 2% of all the studies carried out in the geriatrics field[37]. Also, the quality of the studies conducted in nursing homes is frequently low[38-42]. This is due to the complexity and heterogeneity of the residents who are characterized by the most dramatic pathophysiological modifications and suffer from chronic conditions accumulated during their entire life. Istitutionalized people show high comorbidity[43,44] and polypharmacy[45,46], they suffer from major geriatric syndromes[47], and they usually display a poor health status[48].

Studies on malnutrition are further complicated by the absence of either standardized criteria for defining malnutrition or gold standard screening tools for testing nursing home residents[49]. The use of different measures makes it difficult to determine the true prevalence of the phenomenon[50,51]. *Table 8* illustrates the different prevalences of malnutrition according to various screening tools as reported in the studies conducted from 2013 to 2014 among nursing homes residents[52].

Table 8: prevalence of malnutrition in the nursing homes according to the various measures used in studies from 2013 to 2014

Measure	Prevalence
Weight loss: >5% in 30 days or >10% in 6 months	1.5–11%
Weight loss: ≥1 kg in last 3 months	12%
Weight loss: ≥5% in the last 3 months or ≥10% in the last 6 months	11.9%
Weight loss in the last 3 months	43%
Weight loss 1–3 kg	19.3%
Weight loss >3 kg	6.2%
Unintentional weight loss	17.1%
BMI <18.5	5–37%
BMI <19	12%
BMI <20	8.5–22.1%
BMI <21	15–26.6%
BMI <22	21.66–41%
MNA – malnourished[a]	5.9–38%
MNA-SF – malnutrition[b]	15.9–30%
MNA ≤11	66.5%
Low food intake	21.3%
Food intake <25% of meal	22%
≥25% of food left uneaten after each meal	51.2%
Loss of appetite	6.4%
Malnutrition: one of three criteria (BMI, weight loss, or oral intake)[c]	18.9–24%
MUST – high risk of undernutrition[d]	8.6–13%
GNRI – high risk of malnutrition[e]	36%
NRS[f]	8.6%
SNAQ – malnourished[g]	12.9%
Overall clinical impression[h]	24.1%

GNRI, Geriatric Nutritional Risk Index; MNA, Mini-Nutritional Index; MNA-SF, mini-nutritional status – short form; MUST, malnutrition universal screening tool; NRS, nutritional risk screening; SNAQ, Short Nutritional Assessment Questionnaire.
[a]MNA less than 17 indicates malnutrition.
[b]MNA-SF of 7 or less indicates malnutrition.
[c]Malnutrition: one of three criteria: BMI of 20 or less; unintentional weight loss of at least 6 kg in the last 6 months or at least 3 kg in last month; and no nutritional intake for 3 days or reduced intake for more than 10 days combined with BMI 21–23.
[d]MUST based on BMI, percentage weight loss during the last 3–6 months, and acute disease (range 0, 1, or 2 with 0 = low risk of malnutrition, 2 = high risk of malnutrition).
[e]GNRI – based on albumin, weight, and ideal body weight: high risk of malnutrition GNRI less than 92; low risk GNRI 92–98, and no risk GNRI greater than 98.
[f]NRS 2002 – BMI, weight loss, oral food intake, and acute disease; total score of at least 3 is nutritional risk, less than 3 is recommend weekly re-screening, no risk if all are no.
[g]SNAQ: unintentional weight loss (>3 kg/month), decreased appetite in last month and use of supplemental drinks or tube feeding in last month: well nourished, moderately malnourished and severely malnourished.
[h]Evaluator's clinical impression of malnutrition: global subjective clinical assessment for malnutrition.

Regardless the tool used, screening for malnutrition is recommended among all istitutionalized older people. Screening should be carried out on admission and then monthly. People at risk for malnutrition should be screened more frequently, according to the subject's clinical status and the degree of risk[53].

The etiology of malnutrition among residents is heterogeneous. Modifiable factors should be promptly identified to target solutions. *Table 9* synthesizes the principal predisposing factors[54].

Table 9: malnutrition risk factors

Risk factor	Possible causes
Psychological, social and environmental	Social isolation Grieving Financial difficulties Ill-treatment Hospitalization
Oral and dental care disorders	Mastication disorders Poor dental status Poorly fitting dentures Dryness of the mouth Oropharyngeal candidiasis Dysgeusia
Swallowing disorders	Ear, nose and throat diseases Vascular, neurodegenerative diseases
Psychiatric disorders	Depressive syndromes Behavioural disorders
Dementia	Alzheimer's disease Other forms of dementia
Other neurological disorders	Delirium Parkinsonism
Polypharmacy	Especially medications causing: -dysgeusia -dryness of the mouth -gastro-intestinal disorders -anorexia -drowsiness Long term corticosteroid therapy
Any acute disorder or decompensation of a chronic disease	Pain Infectious disease Fractures Surgery Severe constipation Pressure sores
Dependency for daily activity	Eating dependency Mobility dependency
Restrictive diets	Salt-free Slimming Diabetic Cholesterol lowering Long-term residue free diets

Malnutrition and physical performance

During chronic malnutrition the organism tries to preserve its muscle mass by using mainly the adipose tissue as primary energy source[55]. Anyway, fat mass cannot provide the necessary amino acids for the energy needs of the glycolytic tissues and the brain. Therefore, a variable degree of muscle catabolism occurs[56,57] leading to muscle atrophy and impaired muscle function (reduction of muscle strength[58], and power[59]).

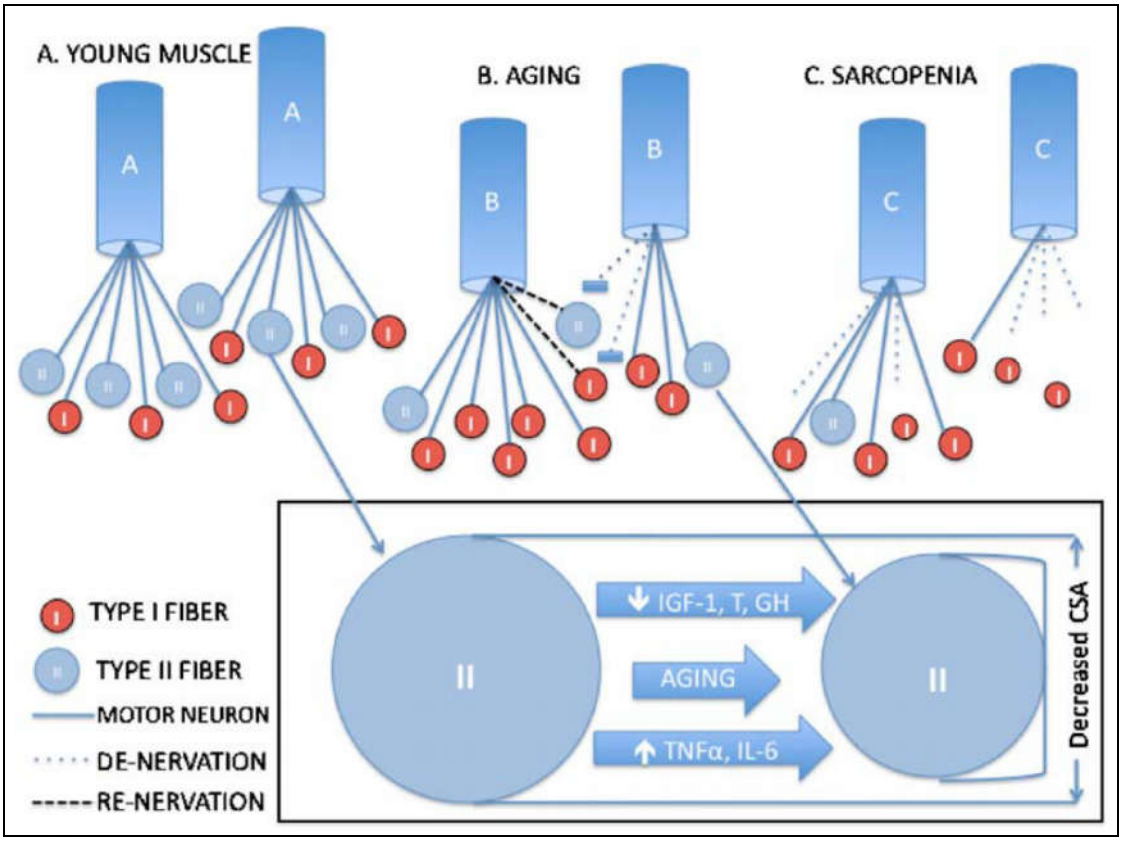
Even if the muscle mass is the major source of protein also some organs like the heart and lungs are partially broken down to provide the required amino acids. This contributes to impair cardiovascular fitness[56,60,61] and diminish the dynamic physical performance of the organism. Decreased muscle power has been found to be a predictor of physical performance[59].

Skeletal muscle power is the product of the force and the contraction velocity. It physiologically reduces with ageing at a faster rate than muscle strength and mass[62].

Both changes in muscle quantity and quality (adipose infiltration) alter muscle power. In particular the age-related muscle atrophy involves preferentially type II myofibres[63] which are more important for rapid strength[64] and power generation than type I fibres[65]. The impairments in the neuromuscular system should also be considered as contributors to the reduction in muscle power[66]. Indeed, a positive association between the measures of muscle power and EMG rise have been demonstrated[67].

Figure 6 illustrates the reduction in type II muscle fibres and motor neuron denervation related to ageing and malnutrition associated sarcopenia[68].

Figure 6: changes in the motor unit from young muscle, to aging to malnutrition associated sarcopenia



IGF-1 Insulin-Like Growth Factor-1; GH Growth Hormone; TNFα Tumor Necrosis Factor alpha; IL-6 Interleukin 6; CSA Cross Sectional Area

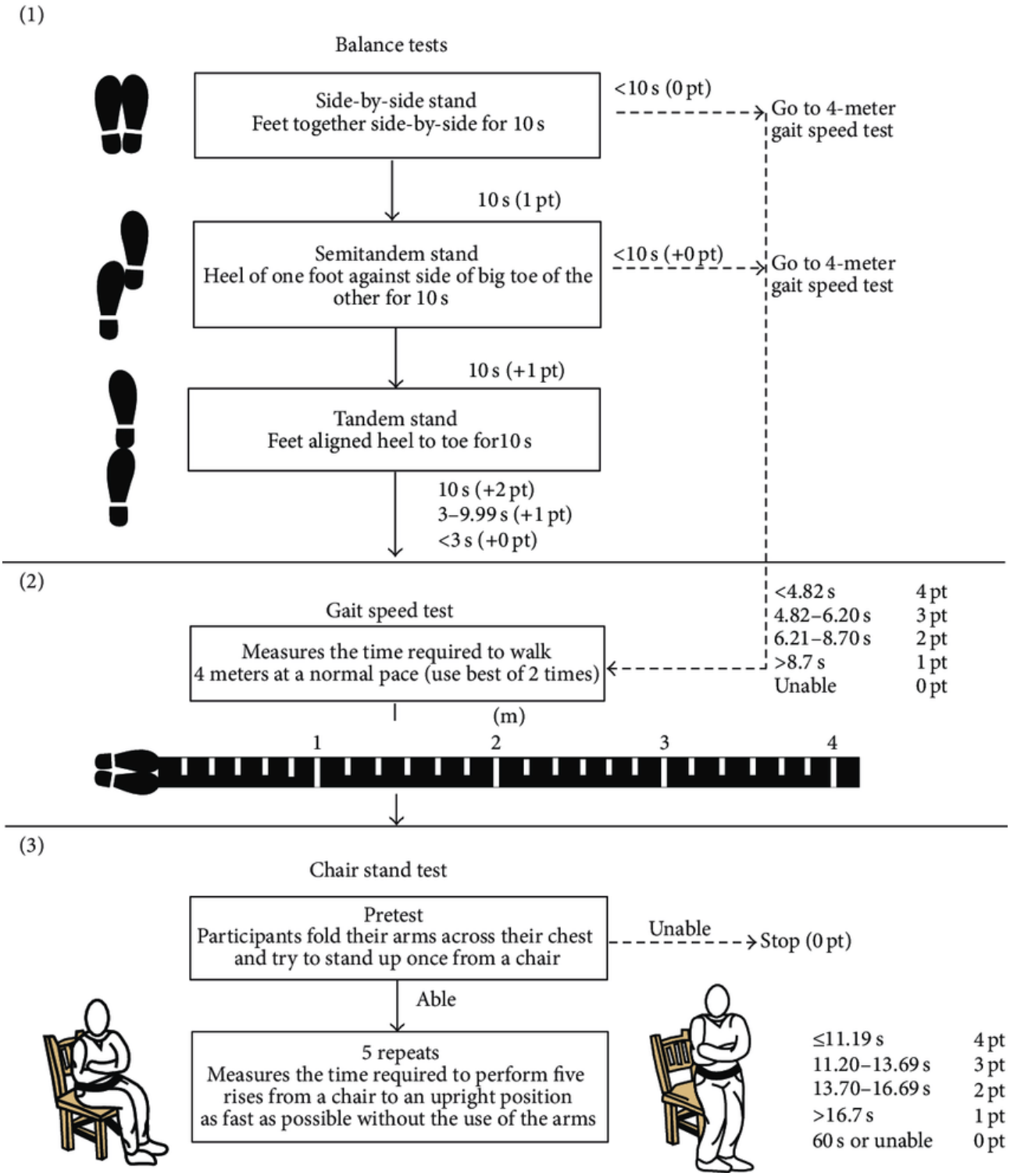
Since in older adults muscle power declines more rapidly than strength and mass, it is the most discriminant predictor of functional performance also under pathologic conditions (i.e. malnutrition)[67].

The Short Physical Performance Battery (SPPB)[69] (*Figure 7*) has been used in many studies to assess functional performance in older adults[70-74].

The SPPB is composed by three subtests: balance tests, gait speed and chair stand tests.

For the standing balance test, the subject is asked to stand in three increasingly challenging positions for 10 s each: a side-by-side-feet standing position, a semi-tandem position, and a full tandem position. For the gait speed subtest, the subject is asked to walk at his usual pace over a 4-m course, beginning with a stationary start. The faster of the two trials (time in seconds) is subsequently used for the calculation of the summary score. For the chair-stand subtest, the subject is asked to rise and sit from a chair five times as quickly as possible with hands folded across the chest. This performance is expressed as a total time (in seconds) to complete the test. The results of the three timed tasks are scored from 0 (worst performers) to 4 (best performers) according to predetermined cut-points. The sum of the scores from the three subtests generates a physical performance summary score ranging from 0 (worst performance) to 12 (best performance).

Figure 7: the short physical performance battery



While the balance test is a measure of static physical performance the gait speed and chair test are dynamic measures.

Muscle power could be better reflected by dynamic physical performance tests. Indeed, reduced muscle power has been associated to a lower gait velocity and worse performance in the chair stand test[73]. Moreover, muscle power also proved to influence also the performance of the static subtest of the SPPB, as demonstrated by Mayson and coworkers[75]. Therefore, it is not surprising that higher contraction velocity was associated with a higher SPPB total score[67].

The INCUR study

The "Incidence of pNeumonia and related ConseqUences in the nursing home Residents" (INCUR) study was an observational longitudinal cohort study aimed at retrieving data from routine clinical practice in order to estimate the incidence of pneumonia events in older people living in a sample of French nursing homes[76]. The INCUR was also designed to estimate the clinical and economic consequences of pneumonia events by measuring the subsequent access to medical procedures and resources.

According to predefined sample size analyses[76] 800 residents of 13 nursing homes randomly selected in the French Midi-Pyrénées region were recruited. The Nursing homes of the Midi-Pyrénées region were consecutively and randomly invited at participating in INCUR. After that each nursing home had accepted to be involved in the study, all residents (according to their eligibility for INCUR) were assessed by the study personnel. The recruitment was conducted up to the reaching of the final sample of 800 participants. All the nursing homes were part of a national network of institutions representative of this healthcare in France[37]. To be part of the project, the director, the coordinating physician, and the responsible for the nursing of each institution signed a formal agreement and letter of support.

The main inclusion and exclusion criteria were the score obtained at the Autonomie Gérontologie - Groupes Iso-Ressources (AGGIR) scale by the participant This scale allows to homogeneously generate six Groupes Iso-Ressources (GIR) at the French national level. The resulting GIR expresses the global functional capacity of the person and drives decisions
about the provision of social support from the public healthcare system. People with severe disability were excluded from INCUR on the basis of the worst GIR group (i.e., 1). The reason for such exclusion was the impossibility to determine the patients' weight of functional loss due to a pneumonia event (primary aim). Similarly, residents with no sign of functional impairment at the

AGGIR scale (that is having the maximum GIR score of 6) were excluded due to the incapacity to perceive possible functional improvement over the follow-up.

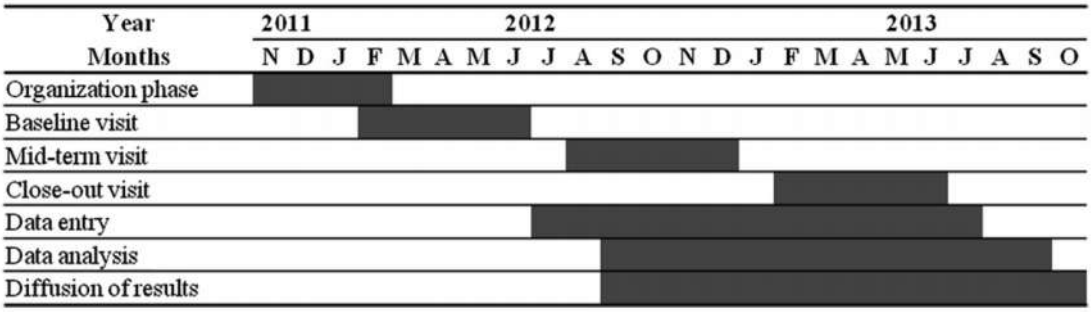
Table 10 illustrates the inclusion and exclusion criteria of the study.

Table 10: inclusion and exclusion criteria of the INCUR study

Inclusion criteria	- Residents aged 60 years and older - *Groupes Iso-Ressources* (GIR) ranging between 2 (included) and 5 (included). This is the French administrative tool used to rate the ability of the person to be independent; it ranges from 6 (fully independent) to 1 (fully dependent, bed-ridden)
Exclusion criteria	- Residents living in the participating nursing homes for less than 30 days since the baseline study visit - Refusal of the patient and/or the family to participate at the INCUR project

Each eligible participant was followed-up for 12 months with a total of three clinical assessments: at baseline, 6 months (mid-term visit), and 12 months (close-out visit). The timeline of the INCUR study is depicted in *Figure 8*. Recruitment of the participants and baseline visits began in February 2012 and ended in July 2012, after a preliminary organization phase (for coordinating the researchers' activities with the participating nursing homes).

Figure 8: the timeline of the INCUR study



The INCUR visits were conducted by research staff specifically trained at the Gérontopôle of Toulouse. The evaluations used multiple scales, questionnaires and tests based on the Geriatric Minimum Data Set (GMDS)[77], thus allowing a comprehensive assessment of the participants. The GMDS is a package of assessment tools designed by a multidisciplinary task force group (i.e., the Gerontonet)[78], aimed at evaluating the different areas of the person's health, including physical function, nutrition, cognition, depression and quality of life. As shown in *Table 11*, these include: ADL[79], Instrumental ADL (IADL)[80], European Quality of Life (EuroQoL) instrument[81], frailty phenotype proposed by Fried and colleagues[82], Abbreviated Mental Test[83], 10-item Geriatric Depression Scale[84], Mini Nutritional Assessment[85].

Table 11: main areas investigated and related instruments adopted in the INCUR study

Area	INCUR assessment
Sociodemographics	
Body composition	Anthropometric measures
Anamnesis/Comorbidity	Current diseases
Medications	
Vaccinations	Influenza and pneumococcal vaccine
Cognition	Abbreviated Mental Test
	Geriatrics Depression Scale
Quality of life	Euro-QoL 5D
Pain	Pain Visuo-Analogic Scale
Functional Status	Activities of Daily Living
	Instrumental Activities of Daily Living
	Short Physical Performance Battery
	Hand grip strength
Nutrition	Mini Nutritional Assessment
Healthcare cost	Data from the *Caisse Primaire d'Assurance Maladie*
Follow-up	Intercurrent diseases
	Therapy modifications
	Hospitalization events
	Death events and causes of death

The GMDS instrument was originally conceived to promote the translation of routinely collected clinical parameters into research data. Therefore, consistently with the descriptive nature of the INCUR study, the items collected were primarily retrieved from the medical charts of the participants (if present). Missing data were completed by specific evaluations of the INCUR study staff.

The same standardized multidimensional assessment performed at the baseline visit was then repeated at the 6-and 12-month follow-up visits. Additionally, the follow-up visits were specifically focused at identifying the onset of major health-related events (in particular pneumonia) occurred during the previous 6 months of follow-up. In particular, the study staff retrieved information about major intercurrent illnesses, emergency room admissions, hospitalizations, and death events

(including causes) from the patients' medical records and charts, the nursing home personnel, and the proxies of the participant. Moreover, in between the follow-up visits, regular contacts between the study staff and the nursing homes personnel were maintained in between the follow up visits to facilitate and improve the identification of the health-related events experienced by the INCUR participants.

To design and develop the INCUR study, the principles of the Declaration of Helsinki were followed and ethical standards complied. The Ethics Committee of the Centre Hospitalier Universitaire de Toulouse and the Consultative Committee for the Treatment of Research Information on Health (CNIL) approved the entire study protocol. The Ethics Committee waived the need for written informed consent from the participants given the epidemiological nature of the research within the domain of current clinical practices. Therefore, the participants were not required to provide a written informed consent to the study, but all participants received written information about the ongoing research (including its objectives and procedures) by the study investigators. The residents were then free to exclude their data from the collection or analysis at any time. In case of residents with cognitive impairment or unable to understand the research protocol, proxies were informed.

PREMISES AND OBJECTIVE OF THE STUDY

Malnutrition is a geriatric syndrome associated with many adverse clinical outcomes[5,8,33]. It is particularly prevalent among institutionalized older people[7]. In fact, data estimate that 15.9-30% of nursing home residents present a malnutrition profile when screened by using the Mini Nutritional Assessment Short Form (MNA-SF) questionnaire[86].

Malnutrition generates energy and nitrogen negative balance which progressively depletes protein and energy reserves[87-89]. Physical inactivity, highly prevalent among residents, acts with malnutrition synergistically so as to impair muscle health[82,90] and physical performance.

) A relationship between malnutrition and impaired physical performance has been demonstrated[92-95]in community-dwelling people and in individuals referring to geriatric outpatient clinics. However, no study has specifically explored this association among nursing home residents so far. This is perhaps due to the limited physical capacity usually presented by nursing home residents and, more in general, by the still insufficient amount of research conducted in this clinical setting.

Our objective was to investigate the possible link between malnutrition (screened with the MNA-SF) and physical performance (assessed using the SPPB)[69] in older people living in nursing homes. Secondary analyses were aimed at exploring the possible relationship between the single items of the MNA-SF with physical performance, as well as the role of the MNA-SF in the definition of the results of the SPPB subtests.

METHODS

Study design and participants

We used data from the Incidence of pNeumonia and related ConseqUences in nursing home Residents (INCUR) study, a prospective observational cohort composed by 800 nursing home residents, followed over 12 months. The INCUR rationale, study design, and methodology have been previously described[76]. The present analyses were conducted after excluding residents with missing data for the key variables of interest (i.e., MNA-SF, SPPB, or both). The present cross-sectional analyses take advantage of the data collected at the baseline visit.

Nutritional assessment

The MNA-SF[86] is a questionnaire designed to measure the risk of malnutrition and composed by the following six items: A) food intake insufficiency; B) involuntary weight loss; C) mobility impairment; D) recent psychological stress or acute disease; E) neuropsychological problems (i.e. dementia or depression); and F) abnormal body mass index (BMI). In case of missing value for the BMI, the measurement of the calf circumference can be used in substitution. The MNA-SF score can range between 0 and 14 points with higher values indicating better nutritional status. Scores between 8 and 11 points identify a population at risk of malnutrition, whereas values ≤ 7 are suggestive of malnutrition[86]. MNA-SF has a strong correlation with the full MNA[29,30], but it has also been validated as an independent tool for nutritional screening in older adults and in particular in nursing home residents[29,30].

Outcome measures

Physical performance was assessed using the SPPB[69]. The SPPB is a physical performance test composed by three timed subtasks: 4-meter usual gait speed, balance, and chair stand tests. Timed

results (in seconds) from each test are categorized from 0 (worst performers) to 4 (best performers) points, according to validated and standardized cut-points[69]. The sum of scores from the three subtests generates a summary score of physical performance ranging from 0 to 12. The SPPB has been in use for more than 30 years, and shown to be a strong predictor of major health-related outcomes in older persons, including disability, hospitalization, institutionalization, and mortality[96].

Covariates

At baseline, socio-demographic information, medical history, and comorbidities were recorded. The clinical conditions presented by the individual were used to compute the Charlson Comorbidity Index (CCI)[97] (*Table 12*). The CCI is a method of categorizing comorbidities of patients. Each comorbidity category has an associated weight (from 1 to 6), based on the adjusted risk of mortality or resource use, and the sum of all the weights results in a single comorbidity score for the patient. A score of zero indicates no comorbidity. The higher the score, the more likely the predicted outcome will result in mortality or higher resource use[97].

Weight and height were measured and BMI calculated. Calf circumference and hand grip strength were also registered. Activities of Daily Living (ADL)[79] and Instrumental ADL (IADL)[80] described the functional status of the participants. The cognitive function was evaluated with the Abbreviated Mental Test (AMT) scale[83].

Table 12: Charlson Comorbidity Index

Comorbid conditions	Weight
Myocardial Infarction	1
Congestive Heart Failure	1
Peripheral Vascular Disease	1
Cerebrovascular Disease	1
Dementia	1
COPD	1
Connective Tissue Disease	1
Ulcer Disease	1
Mild Liver Disease	1
Diabetes Mellitus	1
Hemiplegia	2
Moderate or Severe Renal Disease	2
Diabetes Mellitus with End- Organ Damage	2
Any Tumour	2
Leukaemia	2
Lymphoma	2
Moderate or Severe Liver Disease	3
Acquired Immune Deficiency Syndrome	6
Metastatic Solid Tumour	6

Statistical analyses

Linear regression analyses were used to study the association between nutritional status (MNA-SF total score) and physical performance (SPPB). Unadjusted and adjusted models were performed. Analyses were adjusted for age, sex, education and those factors potentially affecting physical performance, such as cognitive difficulties (assessed through the AMT) and comorbidities (evaluated with the CCI).

Secondary analyses were performed to assess which item of the MNA-SF was most strongly associated with physical performance. To allow a fair comparison among the different regression coefficients (thus, predictors of interest), each independent variable was rescaled for its standard deviation (SD). First each item of the MNA-SF was tested as predictor of physical performance in

unadjusted and adjusted (age, sex, education, AMT and CCI) linear regression models. Then an exploratory model taking into account all the items of the MNA-SF and the covariates as predictors of the SPPB score was used to explore which item of the MNA-SF displayed the strongest association with physical performance. Since the item-by-item analyses had just an exploratory nature, the level of statistical significance was not changed and no correction for multiple testing was performed.

Linear regression analyses were also used to explore the association of the MNA-SF with each subtest of the SPPB (expressed as a score ranging from 0 to 4). All statistical analyses were conducted using SPSS (Statistical Package for the Social Sciences), version 26.0 (SPSS Inc. Chicago, IL, USA).

RESULTS

The sample included 499 individuals, after excluding the residents with missing data for the MNA-SF (n=5), SPPB (n=280), or both (n=16). Excluded individuals were more compromised, cognitive impaired and depressed than the included ones. In particular they displayed a higher risk of malnutrition according to the MNA-SF scores. Moreover, their muscle strength and mass were more reduced with a consequent worse performance in their activities of daily living. Finally, their quality of life was lower in spite of a minor level of pain (*Table 13*).

Table 13 illustrates the main characteristics of the studied population and of the excluded residents. Mean age of the included sample was 85.80 (SD 7.20) with a higher prevalence (73.10%) of women. The mean MNA-SF score was 10.35 (SD 2.22), overall characterizing the population as at risk of malnutrition. Interestingly, the mean BMI was still within the normal range (25.27 kg/m^2, SD 5.32). The mean handgrip (14.27 kg, SD 7.88), SPPB score (3.05, SD 2.65) and usual gait speed (0.55 m/s, SD 0.23) were consistent with a severe physical impairment and muscle weakness. However, the mean value of calf circumference (33.49 cm, SD 3.99) tended to be within the range of normality (≥ 31.0 cm). Instead mean ADL (2.96, SD 1.77) and IADL (0.75, SD 0.74) scores confirmed the reduced functional ability of our sample.

Table 13 main characteristics of the included and excluded residents

Variables	Number of patients (n=499)	Number of patients (n=301)	p
Age (years), mean (SD)	85.8 (7.20)	86.69 (8.09)	0.11
Gender (women), number (%)	364 (73.10)	226 (75.83)	0.24
Education (years), mean (SD)	8.46 (3.29)	8.49 (3.15)	0.92
Marital status, number (%)			
married	67.0 (13.60)	32 (10.7)	0.06
single	83.0 (16.80)	51 (17.11)	
widow/widower	318.0 (64.5)	181 (60.73)	
divorced	25.0 (5.10)	29 (9.73)	
Smoking (current), number (%)	18 (3.6)	2 (0.7)	0.04
Alcohol consumption (current), number (%)	6 (1.2)	3 (1.0)	0.64
Height (cm), mean (SD)	159.08 (8.60)	159.52 (8.31)	0.54
Weight (kg), mean (SD)	63.87 (14.37)	63.87 (14.37)	0.99
BMI (kg/m^2), mean (SD)	25.27 (5.32)	25,09 (5.25)	0.69
MNA-SF, mean (SD)	10.35 (2.22)	8,76 (2.40)	<0.001
Calf circumference, mean (SD)	33.49 (3.99)	32,45 (4,53)	0.002
Hand grip (kg), mean (SD)	14.27 (7.88)	10.93 (7.55)	<0.001
Gait speed (seconds), mean (SD)	0.55 (0.23)	0.63 (0.3)	0.38
SBBP Total score, mean (SD)	3.05 (2.65)	4.0 (2.28)	0.39
ADL, mean (SD)	2.96 (1.77)	1.41 (1.33)	<0.001
IADL, mean (SD)	0.75 (0.74)	0.42 (0.60)	<0.001
CCI, mean (SD)	2.33 (2.01)	2.49 (2.07)	0.31
AMT, mean (SD)	5.89 (2.53)	4.89 (3.55)	<0.001
GDS, mean (SD)	2.59 (2.25)	3.57 (2.62)	<0.001
Number of drugs, mean (SD)	8.51 (3.96)	8.37 (4.32)	0.65
Quality of Life (0–100)*, mean (SD)	68.7 (25.48)	62.57 (27.19)	0.03
VAS (0-100), mean (SD)	61.84 (33.13)	51.68 (33.88)	0.01

SD: standard deviation; m: meter; kg: kilograms; cm: centimetres; s: second; BMI: body mass index; MNA-SF: Mini Nutritional Assessment Short Form; SPPB: Short Physical Performance Battery; ADL Activities of Daily Living; IADL Instrumental Activities of Daily Living; CCI: Charlson Comorbidity Index; AMT: Abbreviated Mental Test; GDS Geriatric Depression Scale; VAS Visual Analog Scale

Unadjusted (B 0.39, 95% CI 0.3-0.5, p <0.001) and adjusted (B 0.38, 95% CI 0.2-0.5, p <0.001) linear regression analyses demonstrated a direct association between the MNA-SF questionnaire and physical performance.

In the analyses exploring the association of the individual components of the MNA-SF with physical performance, food intake insufficiency, weight loss, mobility impairment, recent psychological stress or acute disease and small calf circumference were all predictors of low physical performance. However, after adjustment for potential confounders, weight loss and calf circumference were not significant predictors anymore (*Table 14*).

Table 14 unadjusted and adjusted linear regression analyses exploring the association of SPPB with the single items of MNA-SF

SPPB			
UNADJUSTED ANALYSES			
	B	**95% C.I.**	**p**
Food intake/SD	0.42	0.19 - 0.65	< 0.001
Weight loss/SD	0.34	0.11 - 0.57	0.004
Mobility/SD	1.09	0.87 - 1.3	< 0.001
Recent psychological stress or acute disease/SD	0.36	0.13 - 0.59	0.003
Neuropsychological problems/SD	0.16	-0.07-0.40	0.16
BMI/SD	-0.03	-0.27-0.2	0.77
Calf circumference/SD	0.25	0.02 - 0.49	0.04
ADJUSTED ANALYSES			
	B	**95% C.I.**	**p**
Food intake/SD	0.34	0.03 - 0.65	0.03
Weight loss/SD	0.28	-0.01 - 0.58	0.06
Mobility/SD	1.15	0.86 - 1.44	< 0.001
Recent psychological stress or acute disease/SD	0.37	0.04 -0.69	0.03
Neuropsychological problems/SD	-0.11	-0.50 - 0.29	0.58
BMI/SD	-0.08	-0.38 - 0.23	0.62
Calf circumference/SD	0.09	-0.21 - 0.39	0.56

**Adjusted analyses for age, sex, education, Abbreviated Mental Test, Charlson Comorbidity Index*

SPPB: Short Physical Performance Battery; SD: standard deviation; BMI: Body Mass Index

In the multiple exploratory model only mobility impairment (B 1.13, 95% CI 0.85-1.42, p <0.001) and recent psychological stress or acute disease (B 0.42, 95% CI 0.11-0.73, p <0.008) predicted the SPPB score (*Table 15*).

Table 15 multiple exploratory model evaluating all the items of the MNA-SF and the covariates as predictors of the SPPB score

SPPB				
Variables	**B**	**95% C.I.**		**p**
Age	-0.11	-0.15	-0.07	< 0.001
Sex	-0.16	-0.82	0.50	0.63
Education	0.04	-0.04	0.12	0.35
CCI	-0.03	-0.17	0.10	0.65
AMT	0.12	0.01	0.23	0.04
Food intake/SD	0.18	-0.12	0.48	0.24
Weight loss/SD	0.21	-0.06	0.49	0.13
Mobility/SD	1.13	0.85	1.42	< 0.001
Recent psychological stress or acute disease/SD	0.42	0.11	0.73	0.01
Neuropsychological problems/SD	-0.16	-0.52	0.20	0.39
BMI/SD	-0.10	-0.38	0.19	0.52
Calf circumference/SD	0.06	-0.22	0.34	0.68

SPPB: Short Physical Performance Battery; SD: standard deviation; CCI: Charlson Comorbidity Index; AMT: Abbreviated Mental Test BMI: Body Mass Index

Despite the poor results at the SPPB reported by our sample, the MNA-SF score was significantly related to all the three subtests of the SPPB (*Table 16*). The association was particularly strong between MNA-SF and gait speed.

Table 16 unadjusted and adjusted linear regression analyses of the association of the subtests of the SPPB with the MNA-SF

UNADJUSTED ANALYSES			
Walking speed (Score 0-4)			
	B	**95% C.I.**	**p**
MNA-SF	0.17	0.12 - 0.22	< 0.001
Chair stand test (Score 0-4)			
MNA-SF	0.05	0.03 - 0.08	< 0.001
Balance test (Score 0-4)			
MNA-SF	0.17	0.13 - 0.22	< 0.001
ADJUSTED ANALYSES			
Walking speed (Score 0-4)			
	B	**95% C.I.**	**p**
MNA-SF	0.18	0.11 - 0.25	< 0.001
Chair stand test (Score 0-4)			
MNA-SF	0.05	0.01 - 0.10	0.01
Balance test (Score 0-4)			
MNA-SF	0.15	0.07 - 0.22	< 0.001

**Adjusted analyses for age, sex, education, Abbreviated Mental Test, Charlson Comorbidity Index*

SPPB: Short Physical Performance Battery; MNA-SF: Mini Nutritional Assessment Short Form

DISCUSSION

In this cross-sectional study, we found that nutritional status (screened with the MNA-SF) was a significant predictor of physical performance (assessed through the SPPB) in a sample of older people living in a nursing home. The MNA-SF was also significantly associated with all the three SPPB subtests, in particular with the gait speed. Moreover, 3 out of 6items of the MNA-SF (decreased food intake, mobility impairment, recent psychological stress or acute disease) were independently associated with physical performance. This association was also proved in a multiple exploratory model for the MNA items which reflect more the general health status: mobility impairment and recent psychological stress or acute disease.

Our study confirms the association between malnutrition and the SPPB impairment, previously found in acute geriatric patients[98], community-dwelling older adults[92-94], and in the home care setting[95]. The extension of this relationship to the complex population represented by nursing home residents is of paramount importance. The number of people living in nursing homes is expected to rise in the next decades due to the rapid aging of the World population. However, research in this geriatric field is still scarce; thus, studies conducted in such a context fill in a gap of knowledge providing information for evidence-informed clinical practice.

Nutritional problems are common among institutionalized older people. Previous data from the INCUR cohort showed that about two thirds of the residents were either at risk of developing malnutrition (58.7%) or already malnourished (15.7%)[99].

Malnutrition alters body composition but reduction in muscle function (i.e. strength or performance) is evident before muscle mass declines[100]. Indeed, in our sample, the majority of people (76.5%) had an impaired physical performance (SPPB score <5) in spite of normal calf circumference and BMI values.

We found that in people living in nursing homes their nutritional status screened by the MNA-SF was associated with physical performance. In such a context characterized by extremely vulnerable, comorbid and disabled people both malnutrition and physical impairment were highly prevalent exerting a mutual negative influence. The low intake and uptake of nutrients compromise muscle protein synthesis and activate catabolic pathways[101]. On the other hand, older people suffering from multiple diseases are frequently bedridden and inactivity induces resistance to muscle anabolic stimuli. Moreover, inflammatory cytokines, typical of pathologic conditions, have a dual negative effect on muscles: the stimulation of catabolic processes[102] and the anorexizing effect[103].

When analyzing the association between nutritional status and physical performance it should also be considered the characteristics of the tools used to assess this relation.

The MNA-SF is composed by both nutritional and general geriatric items. In particular it includes a mobility item which indeed demonstrated to have the strongest association with physical performance. Moreover, MNA has a multidimensional nature making it highly informative on the global health status of the individuum. Not surprisingly, it has shown to be able to identify people at risk of developing adverse clinical events[104], and it has been proposed as a frailty instrument[105,106]. Our results that show the association of the SPPB with the MNA-SF are consistent with and support these previous findings. They also confirm how the assessment of malnutrition is embedded in the overarching construct of physical frailty.

Screening for both malnutrition and physical performance is important to prevent their adverse consequences[107,108]. However, physical performance measures are not routinely used in nursing homes. The reasons are manifold: physicians who should perform the screening frequently complain about a lack of time. Moreover, physical performance tests may be too though to be implemented in the institutionalized population.

The MNA-SF, when analysed in its parts, allows an easy and quick evaluation of locomotion, humoral and clinical aspects although it has been traditionally seen as a unique result. Therefore, it might cost-effectively improve the assessment of the risk profile of the complex individuals living in nursing homes. It is particularly suitable for bedridden people and individuals with an elevated degree of impairment who are unable to be screened with the classical physical performance tests. The MNA-SF could thus be considered a frailty screening instrument to guide ad hoc interventions whose implementation is still at an early stage in residents of nursing homes[109,110].

Our results are consistent with the proven association between nutritional status and functional decline in istitutionalized older people[111,112]. Moreover, we confirmed the role of the MNA-SF as a multidimensional instrument able in identifying individuals with reduced physical performance, who are more vulnerable to adverse clinical events.

Some limitations are worth mentioning. The cross-sectional design prevents to demonstrate causality in the studied relationship. The nutritional status was based on the MNA-SF that, although represents a well-established and widely validated instrument, may still be suboptimal at capturing the phenotypic aspect of the individual (and, for example, not his/her biological status). Finally, we cannot exclude that third factors not considered in the present analyses might differently explain our findings (e.g., level of physical activity, nutritional supplementation, medications).

CONCLUSION AND IMPLICATIONS

In nursing home residents, the MNA-SF and three of its sub-items (decreased food intake, mobility impairment, recent psychological stress or acute disease) are significantly associated with physical performance, independently of potential confounders. Among the three subtests of the SPPB, MNA-SF was particularly associated with gait speed.

The risk of negative outcomes is high in people living in a nursing home, a setting where malnutrition and physical impairment are extremely frequent. Ad hoc interventions which aim at improving the nutritional status and physical performance should be encouraged for activating a virtuous cycle against further functional decline[105].

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"...·You can't connect the dots looking forward; you can only connect them looking backwards· So you have to trust that the dots will somehow connect in your future· You have to trust in something — your gut, destiny, life, karma, whatever· Because believing that the dots will connect down the road will give you the confidence to follow your heart even when it leads you off the well-worn path and that will make all the difference.....

...·What had been the focus of my entire adult life was gone, and it was devastating...·I really didn't know what to do for a few months...··And so I decided to start over· I didn't see it then, but it turned out that getting fired from Apple was the best thing that could have ever happened to me· The heaviness of being successful was replaced by the lightness of being a beginner again, less sure about everything· It freed me to enter one of the most creative periods of my life...·It was awful tasting medicine, but I guess the patient needed it· Sometimes life is going to hit you in the head with a brick· Don't lose faith· I'm convinced that the only thing that kept me going was that I loved what I did· You've got to find what you love· And that is as true for work as it is for your lovers· Your work is going to fill a large part of your life, and the only way to be truly satisfied is to do what you believe is great work· And the only way to do great work is to love what you do· If you haven't found it yet, keep looking· And don't settle· As with all matters of the heart, you'll know when you find it· And, like any great relationship, it just gets better and better as the years roll on· So keep looking· Don't settle...·

...· for the past 33 years, I have looked in the mirror every morning and asked myself: "If today were the last day of my life, would I want to do what I am about to do today?" And whenever the answer has been "No" for too many days in a row, I know I need to change something· Remembering that I'll be dead soon is the most important tool I've ever encountered to help me make the big choices in life· Because almost everything — all external expectations, all pride, all fear of embarrassment or failure - these things just fall away in the face of death, leaving only what is truly important· Remembering that you are going to die is the best way I know to avoid the trap of thinking you have something to lose· You are already naked· There is no reason not to follow your heart...·· Death is very likely the single best invention of Life· It is Life's change agent· It clears out the old to make way for the new· Right now the new is you, but someday not too long from now, you will gradually become the old and be cleared away· Sorry to be so dramatic, but it is quite true· Your time is limited, so don't waste it living someone else's life· Don't be trapped by dogma — which is living with the results of other people's thinking· Don't let the noise of others' opinions drown out your own inner voice· And most important, have the courage to follow your heart and intuition· They somehow already know what you truly want to become· Everything else is secondary...·

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