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UNIVERSIDADE D
COIMBRA

Catarina Isabel da Costa Ferreira Oliveira Caçador

ASSESSMENT OF NUTRITIONAL STATUS AND DIETARY INTAKE OF INSTITUTIONALIZED OLDER ADULTS

A MULTIDISCIPLINARY APPROACH IN A POPULATION OF RESIDENTS IN VISEU (CENTER OF PORTUGAL)

Tese no âmbito do Doutoramento em Ciências Farmacêuticas, na especialidade de Bromatologia e Hidrologia, orientada pelo Professor Doutor Fernando Jorge dos Ramos e pela Professora Doutora Edite Teixeira de Lemos e apresentada à Faculdade de Farmácia da Universidade de Coimbra.

Janeiro de 2023

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Abstracts

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Caçador C, Teixeira-Lemos E, Oliveira J, Pinheiro J, Ramos F, Veríssimo M, Castilho M. "Physical activity as a mean to maintain independence in older adults in long-term care facilities". Ageing Congress 2018, 27 a 29 Maio 2018. Coimbra

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Caçador C, Teixeira-Lemos E, Oliveira J, Pinheiro J, Mascarenhas F, Martins R, Castilho M. "Medicamentos potencialmente inapropriados e sua possível relação com a dependência em idosos institucionalizados". XIX Congresso da Sociedade Portuguesa de Medicina Física e Reabilitação, 28 a 31 Março 2019. Lisboa

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Resumo

A população idosa em Portugal, em 2021, representava 23,4% de toda a população e as projeções apontam para um aumento neste número. É importante ressalvar que as pessoas com 65 anos ou mais anos não estão distribuídas de forma homogénea pelo território nacional e a Região Centro é uma das áreas mais envelhecidas. A má nutrição causada por excesso ou deficiência de nutrientes é uma condição que afeta os idosos de forma alarmante, principalmente aqueles que vivem em lares. Desta forma, conhecer a rotina alimentar dos idosos – e por consequência a ingestão alimentar e o estado nutricional – é de grande importância. Até ao momento, os estudos publicados que caracterizam o estado nutricional e a dieta de idosos institucionalizados são escassos. Assim, é imperativo retratar a situação atual para potenciar a implementação de medidas adequadas de combate à má nutrição e prevenir estas situações no futuro, melhorando a qualidade de vida. Assim, esta tese de doutoramento teve como principal objetivo avaliar o estado nutricional e o consumo alimentar de idosos institucionalizados em Portugal, mais concretamente no concelho de Viseu, tendo sido feita uma abordagem multidisciplinar destes mesmos idosos.

A revisão sistemática, realizada no âmbito deste trabalho de doutoramento, revelou que um melhor estado nutricional está correlacionado com uma melhoria das capacidades funcionais e cognitivas. Neste trabalho estiveram envolvidos 214 participantes, com uma média de idades de 82,3±6,1 anos, sendo 72% do sexo feminino. A maioria apresentava baixa escolaridade (analfabetos ou até 11 anos de estudo = 94,8%) e eram viúvos, separados ou divorciados (74,3%). A aplicação do Mini Nutritional Assessment (MNA) mostrou que 28% da população idosa estudada estava em risco de má nutrição (sem diferenças significativas entre género) e 57,9% apresentavam excesso de peso (de acordo com o Índice de Massa Corporal – IMC). A má nutrição estava relacionada com um défice de ingestão energética total e de nutrientes sendo as mulheres as mais afetadas. Verificou-se que 75,2% dos idosos apresentaram uma ingestão de proteínas desadequada (39,7% abaixo das recomendações). Também a ingestão de lípidos se revelou desajustada em 30,3%, com 19,6% dos idosos apresentando consumo excessivo. Já relativamente à ingestão dos hidratos de carbono, a maioria (66,8%) está dentro das recomendações. Uma diferença estatisticamente significativa ($p<0,05$) foi encontrada quando se comparou a ingestão energética das mulheres com risco de má nutrição com as que apresentavam estado nutricional normal (1621,2±326,0Kcal/dia vs 1747,3±294,5Kcal/dia, respetivamente). As mulheres sob risco de desnutrição também

apresentaram menor ingestão de proteínas, lípidos, fibras, água, tiamina, ácido fólico, vitamina B12, ácido ascórbico, magnésio, zinco, sódio, potássio e fósforo ($p<0,005$).

Em média, os homens apresentaram perímetro abdominal superior ao das mulheres (101,9±10,0 cm *vs* 94,6±10,5 cm). Os valores do IMC variaram de 16,0 kg/m^2 a 43,3 kg/m^2, com 7,5% dos indivíduos abaixo do peso (IMC <22 kg/m^2), 34,6% com peso normal (IMC 22 – 27 kg/m2), e 57,9% acima do peso (IMC >27 kg/m^2). Os valores do Índice de Barthel (IB) indicaram que a maioria dos participantes no estudo (69,6%) era minimamente dependente nas atividades da vida diária (AVD). Um total de 84 (39,3%) participantes apresentou défice cognitivo, com base no Mini-Exame do Estado Mental (MEEM). As mulheres foram mais afetadas do que os homens ($p<0,01$). Tal como apresentado na revisão da literatura, foi possível demonstrar que o risco de má nutrição (avaliado pelo MNA) está relacionado com menores capacidades funcionais e mentais (segundo o IB e o MEEM) ($p<0,001$). Este estudo também destacou que o IMC, indicador do estado nutricional, se correlacionou com o risco nutricional (avaliado segundo o MNA) ($r=0,28$, $p<0,001$), demonstrando-se a importância da utilização conjunta do IMC e do MNA para a correta avaliação nutricional do adulto mais velho. Este trabalho demonstrou, ainda, que os idosos com maiores níveis de dependência também apresentaram maior probabilidade de défice cognitivo ($r=0,35$, $p<0,0001$).

A polifarmácia e a medicação potencialmente inapropriada (MPI) também são preocupações entre os idosos, principalmente os institucionalizados. Os participantes no estudo tomaram, em média, 7,6±3,3 medicamentos por dia. A polifarmácia foi identificada em 97,9% dos idosos, dos quais 80,8% tomavam 5 ou mais medicamentos por dia e 79,3% dos participantes apresentaram pelo menos uma MPI. A revisão sistemática da literatura identificou uma importante lacuna nos dados que associam os índices de polifarmácia na população portuguesa a outros indicadores da saúde geral. Os idosos que tomavam cinco ou mais fármacos por dia ou que tomavam fármacos do foro psiquiátrico, gastrointestinal ou antidiabéticos orais (independentemente de serem considerados potencialmente inapropriados ou não) apresentaram uma maior probabilidade de apresentarem défice cognitivo ($p<0,05$).

Em conclusão, foi possível destacar que uma avaliação do estado nutricional e de ingestão alimentar dos idosos institucionalizados é essencial para preservar a sua saúde e qualidade de vida; que programas de intervenção multifacetados/ multidimensionais devem ser priorizados, dada a inter-relação que podemos verificar entre o estado nutricional, o estado cognitivo, autonomia e independência dos idosos, especialmente os institucionalizados; que devem ser consideradas intervenções não-farmacológicas de modo a atingir níveis mais elevados de

independência e autonomia, permitindo uma melhoria no autocuidado e bem-estar geral dos idosos; e que uma estratégia global destinada a controlar as perturbações do bem-estar deve incluir a avaliação regular e individualizada dos riscos de desnutrição e seu o diagnóstico precoce.

Finalmente, sugere-se a realização de um estudo mais amplo nos diferentes distritos de Portugal a fim de confirmar (ou não) os dados obtidos em Viseu, nomeadamente no âmbito do novo Instituto Multidisciplinar do Envelhecimento da Universidade de Coimbra.

Abstract

Elderly population in Portugal, in 2021, represented 23.4% of all Portuguese population and this number is foreseen to increase. Importantly, people aged 65 and over are not homogeneously distributed among national territory and the Center Region is one of the most aged areas. Malnutrition either caused by excess or deficiency of nutrients is an alarming condition that affects older adults, especially those living in nursing homes. Knowing seniors' routine diet – and by consequence dietary intake and nutritional status – is of greater importance. To date, the number of published studies that characterize institutionalized elderly nutritional status and diet are scarce. Therefore, it is imperative to picture the current situation to potentiate the implementation of adequate measures to combat malnutrition and to further prevent these situations, improving seniors' quality of life. Thus, this doctoral thesis aimed to assess the nutritional status and dietary intake of institutionalized older adults in Portugal, more specifically in the municipality of Viseu, taking in consideration a multidisciplinary approach.

A systematic review written in the scope of this doctoral work unveiled that better nutritional status is correlated with improved functional and cognitive abilities. Our study had 214 homecare participants, with 82.3±6.1 years-old, and 72% were female. Most of them presented a low educational level (illiterate or 11 years of schooling = 94.8%) and were widowed, separated or divorced (74.3%). This work revealed that 28% of the studied institutionalized population were at risk of malnutrition, according to Mini Nutritional Assessment – MNA (with no significant gender differences) and 57.9% were overweight (according to Body Mass Index – BMI). This reality was related to a deficit of energy and nutrient intake being women the most affected. 75.2% of older adults had inadequate intake of protein (39.7% below recommendations) and 30.3% had inadequate intake of fat (19.6% by excess). Carbohydrates presented an intake of 66.8% according to recommendations. A statistically significant difference ($p<0.05$) in energy intake was found between women at risk of malnutrition and those with a normal nutritional status (1621.2±326.0Kcal/day *vs* 1747.3±294.5Kcal/day, respectively). Women at risk of malnutrition also had lower ingestion of protein, lipids, fiber, water, thiamine, folic acid, vitamin B12, ascorbic acid, magnesium, zinc, sodium, potassium and phosphorus ($p<0.005$).

On average, men had a higher waist circumference (WC) than women (101.9±10.0 cm *vs* 94.6±10.5 cm), but there were no significant differences between men and women in the percentages of participants with WC above the risk cut-offs (102 cm for men and 99 cm for

women). Body Mass Index (BMI) values ranged from 16.0 kg/m^2 to 43.3 kg/m^2 with 7.5% of the subjects being underweight (BMI <22 kg/m^2), 34.6% were normal weight (BMI 22 – 27 kg/m^2), and 57.9% were overweight (BMI >27 kg/m^2). Barthel Index (BI) scores indicated that most patients (69.6%) were minimally dependent on activity of daily living (ADL). A total of 84 (39.3%) participants presented cognitive impairment through the Mini-Mental State Examination (MMSE) screening. Among them, women were more affected than men (p<0.01). The risk of malnutrition (based on MNA scores) correlated with lower functional and mental abilities (based on BI and MMSE scores) (p<0.001), like showed in systematic review. This study also stressed that Body Mass Index (BMI), an indicator of nutritional status, was correlated with nutritional risk (based on MNA scores) (r=0.28, p<0.001), demonstrating the importance of using both BMI and MNA for nutritional evaluation of elderly. Of note, elderly with higher dependency levels also had a higher probability of cognitive impairment (r = 0.35, p<0.0001).

Polypharmacy and potentially inappropriate medication (PIM) are also concerns among elderly people especially in the institutionalized ones. The participants were found to take 7.6±3.3 drugs per day (average ± standard deviation). Polypharmacy was identified in 97.9% of the elderly, 80.8% of which were taking 5 or more medications per day. 79.3% of the participants presented at least one PIM. Besides, our systematic review identified an important gap in data that associates polypharmacy indexes in the Portuguese population with other pillars of general health. This investigation found that patients taking five or more prescription drugs per day (major polypharmacy) or consuming any psychiatric, gastrointestinal, or oral antidiabetic agents (regardless of whether they were considered potentially inappropriate or not) had higher odds of displaying cognitive impairment than those who did not (p<0.05).

So, with our study, it was possible to highlight that nutritional status evaluation and dietary intake were crucial to health preservation and the maintenance life quality; multifaceted/multidimensional intervention programs should be prioritized, given the relationship shown between nutritional status, mental state, independency and autonomy of older adults, specially institutionalized elderly; non-pharmacological interventions should be considered to obtain more independency and autonomy, to allow an improvement in self-care and general well-being of older adults; and a global strategy to control perturbations in well-being should include a regular and individualized evaluation of risks of malnutrition and its early diagnosis.

Finally, it is suggested the realization of other studies in different districts of Portugal, in order to confirm (or not) the data obtained in Viseu, namely in the scope of the new Multidisciplinary Institute of Elderly in Coimbra University.

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Abbreviations

ADLs	Activities of Daily Living
AI	Adequate Intake
AR	Average Requirements
BI	Barthel Index
BMI	Body Mass Index
CI	Confidence Interval
DRI	Dietary Reference Intake
EFSA	European Food Safety Authority
ESPEN	European Society of Clinical Nutrition and Metabolism
GDS	Global Deterioration Scale
GNRI	Geriatric Nutritional Risk Index
HGS	Hand Grip Strength
INE	*Instituto Nacional de Estatística*
MMSE	Mini-Mental State Examination
MNA	Mini Nutritional Assessment
MNA-SF	Mini Nutritional Assessment Short Form
MUST	Malnutrition Universal Screening Tool
NRS-2002	Nutritional Risk Screening 2002
OR	Odds Ratio
PAL	Physical Activity Level (PAL)
PIM	Potentially Inappropriate Medications
PRI	Population Reference Intake
QoL	Quality of Life
REE	Resting Energy Expenditure
RoB	Risk of Bias

SGA	Subjective Global Assessment
SPMSQ	Short Portable Mental Status Questionnaire
SPPB	Short Physical Performance Battery
W/S/D	Widow/Separated/Divorced
WC	Waist Circumference

General Introduction

Aging is a global and natural phenomenon with long-term implications for society. The increase of elderly is an alarming sociodemographic problem as it strongly impacts population pyramids and economic sustainability [1].

In Europe, by 2050, people aged over 65 are expected to reach 35% of the total population. These numbers are very contrasting to those existing in 1971 where older adults only accounted for 15%. Portugal is no exception. Data from *Instituto Nacional de Estatística* (INE) show an increase in elderly population from 19.0% in 2011 to 23.4% in 2021 (Figure 1.1). Of note, elderly is not equally distributed among Portugal. Region Center and *Alentejo* are the most aged areas in comparison with, for instance, Lisbon metropolitan area (aging index in 2021: 228.6 and 218.6 versus 150.9) [2].

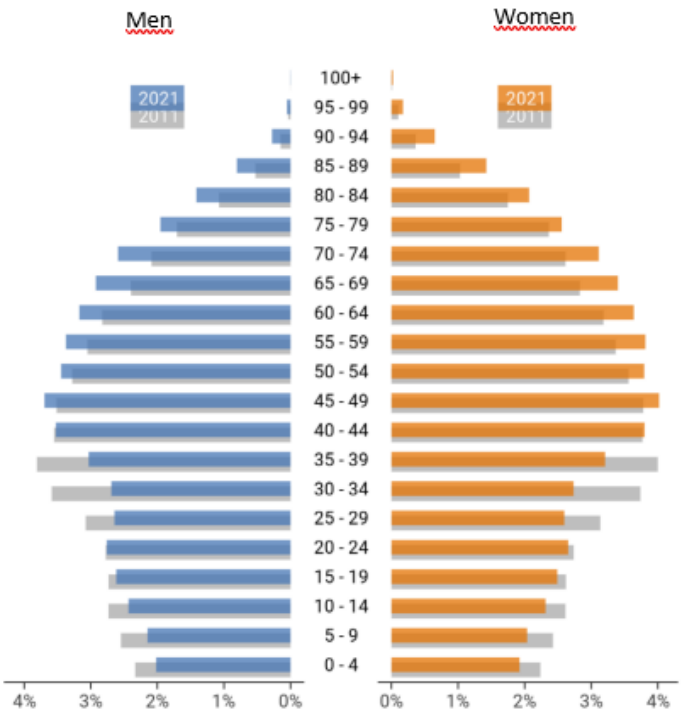

Figure 1.1. Resident population in Portugal according to age group, 2011-2021. Adapted from *Instituto Nacional de Estatística* [2].

With the increase ratio of people aged 65 and over per 100 working-age people (old-age dependency ratio), more pressure is felted on the productive population to support the elderly. Currently, worldwide, the old-age dependency ratio is 12.6%, meaning there is approximately one elderly person for every eight working-age persons. However, data

projects a significant increase close to 50% by 2100 in developed countries, meaning approximately 1 senior for 3 working-age people [3].

This proportion is tendentially augmenting due to several factors such as increased life expectancy and fertility and mortality rates inflection [4]. In fact, from 1960 until 2019, the mean life expectancy in the world increased 20 years while fertility rates have decreased worldwide from 5.0 to 2.4 [5,6]. Improvements in public health care systems and medicines and changes in population lifestyles have led to more individuals surviving until advanced ages [7]. At the same time, the widespread use of contraception and family planning programs to reduce the incidence of unplanned pregnancy coupled with the instability of modern partnerships and the higher cost of maintaining a family together impact the fertility rate, modifying demographics cohorts [8].

Age and the prevalence of chronic conditions are intrinsically linked, reinforcing the need for long-term care to elderly. Long-term care can either be supported through home services or nursing homes, in addition to periods of lengthy or even recurrent hospital stays. Challenges emerge as current health systems are not prepared to respond to seniors' needs. In line with this, the training of health professionals in geriatric care, the prevention and management of age-related chronic diseases, the development of sustainable policies as well as specialized services will be crucial to respond to the increasing needs of this age group [9].

Thus, in Europe, efforts are being made to implement policies that promote *Active Aging* to avoid disabilities, chronic diseases, and less use of health care services. This concept is defined as "the process of optimizing opportunities for health, participation and security in order to enhance quality of life as people age", approaching the physical, social and mental well-being, as well as, social participation, protection, safety, and care of the elderly [10].

Healthy eating is necessary in all stages of life and essential to support *Active Aging*. In seniors, adequate nutrition achieves greater relevance as it can reduce the impact of these changes on health and improve the quality of life. Nevertheless, depending on the housing context where the elderly is inserted, managing nutritional status can be challenging.

Elderly institutionalization is increasingly a reality in our societies. Recent changes in familiar dynamics and structure are driving more families to resort to institutionalization. Reduced economic resources, the insertion of women in the job market and the absence of physical, and psychological conditions to take care of their relatives are also pointed out as the main reasons for those phenomena [11,12]. This process has a huge negative impact on elderly quality of life, impacting nutritional, functional and cognitive status [13].

Often, the available nutritional support is scarce and, thus, meals are not adapted to the senior needs nor their taste. Several studies demonstrated that a better nutritional status is correlated with improved functional and cognitive abilities, and therefore, with better quality of life. Malnutrition either caused by excess or deficiency of nutrients is an alarming condition that affects older adults, especially those living in nursing homes. With the increasing prevalence of this population cohort in worldwide populations, knowing and understanding their dietary intake and nutritional status is of greater importance.

Thus, the main aim of this work was to assess the nutritional status and dietary intake of institutionalized older adults in Portugal, more specifically in the municipality of Viseu. Hence, and in order to attain this main objective, other secondary objectives were delineated:

(i) evaluate the association between nutrients intake and malnutrition;
(ii) characterize inadequacy of nutrients intake;
(iii) examine the possible relationship between nutritional status and nutritional risk;
(iv) study if nutritional status could be associated with a decrease in functional outcomes for activities of daily living (assessed by BI);
(v) analyze the possible relationship between nutritional status and cognitive impairment (assessed by MMSE);
(vi) assess the prevalence of polypharmacy and potentially inappropriate medications;
(vii) evaluate the possible association between polypharmacy, PIM, cognitive impairment and nutritional status.

To achieve these objectives and better frame the topics in the scope of this thesis, after presenting a general introduction, a brief description of general concepts of aging and nutrition was made.

Thus, in this first chapter, the physiological alterations related to aging were explored as well as the essential concepts regarding nutritional status and dietary intake.

Chapter 2 presents a systematic review performed in accordance with the PRISMA guidelines, aiming to study the potential correlation between nutritional status and polypharmacy, cognitive decline, and functional performance in institutionalized elders. Relevant scientific publications in the last ten years were reviewed and the main findings were presented.

In chapter 3, the nutritional status and dietary intake of institutionalized elderly persons in Viseu, Portugal is reported. An observational study considering the association between energy/nutrients intake and malnutrition and outline nutritional inadequacy is presented in institutionalized older adults concerning dietary intake.

The fourth chapter provided a characterization of the nutritional and functional status of an institutionalized population in one of the most aging regions of Portugal and intended to examine the possible relationship between nutritional status and nutritional risk and whether nutritional status and nutritional risk could be associated with a decrease in functional outcomes for activities of daily living and with cognitive impairment in institutionalized older adults.

In the chapter 5, a study about polypharmacy and potentially inappropriate medication rates in nursing homes residents and their association with cognitive status was presented. Fourteen Portuguese nursing homes in the district of Viseu were analyzed. This chapter intends to be aware of regular, constant, and methodical revision of senior's medical prescriptions that may promote improvements in cognitive outcomes.

The chapter 6 intends to stress and to discuss the major results found in the all the work above presented. It also explored possible avenues of research which can be pursued considering the data presented and future challenges which this research area might face.

The last chapter provide general conclusions derived from this thesis and also future perspectives thought in line with the major conclusions of this work.

The references mentioned throughout this thesis were presented on the last pages.

Finally, a supplementary material was added at the end, with the study approval by the Ethics Committee of Polytechnic Institute of Viseu.

Chapter 1 | Aging and Nutrition: General Concepts

1.1. Physiology of aging

Aging is a spontaneous, progressive, irreversible, and complex biological phenomenon with not only marked alterations at molecular and cellular levels but also with influence in psychological and social spheres [14]. Aging reflects all changes that start with birth, and it does not have to be synonymous with deteriorating health. Thus, there is a clear distinction between healthy and pathological aging. Aging progression depends on genetic and biological characteristics and other modifiable factors such as environmental, psychological, social and lifestyle habits [15]. All these factors directly influence intake nutritional status and consequently the nutritional status of individuals.

In addition to all disadvantages that the aging process may have, there are also positive aspects to be highlighted. By age 65, most of the population is already retired, having a greater time availability, greater freedom, non-compliance to fixed schedules with the possibility of devote to eternally postponed subjects and activities [16]. This population cohort has at the same time a life full of experiences, allowing more concise and enlighten decision. However, the life experience of the elderly is not always properly valued by modern societies, choosing too often for not considering the opinion of these individuals who are always adding value for the life stories they carry.

Healthy aging is inevitably marked by anatomical changes in body composition with a decrease in lean mass that contributes to reduced muscle strength and physical function, increased fat mass, and decreased bone mineral density. Age-associated changes progressively impair self-regulation and regeneration of functional tissues and organs which inevitably leaves the individuals more vulnerable, facilitating the occurrence of pathological processes.

At this stage, significant physiological alterations occur in all major organ systems. Cognition declines; changes in the cardiovascular system result in less cardiac output and higher blood pressure; in the respiratory system, oxygenation starts to be impaired, a decrease in ventilation/perfusion and an increased risk of atelectasis is observed; at the gastrointestinal system there is a delay in gastric emptying and a decrease in gastric liver metabolism; kidney changes result in decreased glomerular filtration rate and less able to control electrolyte homeostasis and finally, in the endocrine system, hormonal changes arise [17].

Additionally, sensory losses may also occur, driving to the decrease of sensations of taste, vision, odor, hearing, and tact, which has a myriad of consequences at general seniors' life

quality. For instance, these changes may influence appetite and the pleasure of eating, cause dysphagia and consequently swallowing difficulties, changes in gastric acidity, constipation, and decreased ability to function of kidneys.

1.2. Nutritional Status

Nutritional status is an important condition that deeply affects elderly general health and reflects the efficiency with which nutritional needs are met. A good nutritional status is achieved when food intake is adequate to meet the nutritional needs of the individual.

Food intake declines naturally with age derived from physiological age-induced changes, regardless of chronic illness and disease. Nutritional changes are also adapted and it is observed a decrease in energy needs and an increase in protein and micronutrients [18]. In fact, eating patterns alterations were identified with age in observational studies [19,20]. Retirement in women has led to healthier food habits while similar improvements were less observed among men [21]. Similarly, analysis of food consumption in a British birth cohort reflected a healthier diet in later years with the replacement of white bread by granary and whole meal bread, lower consumption of red and processed meats, higher consumption of fish and vegetables and lower consumption of coffee [20].

However, sensorial alteration may also exacerbate the lack of appetite, ultimately leading to nutritional inadequacy and increased risk of undernourishment [21–23]. Furthermore, physiological alterations also lead to insufficient ingestion and deficient absorption of essential nutrients in older people [24]. Therefore, the preservation of optimal caloric intake is a key factor in the general health of elderly.

Nutritional status maintenance in institutionalized elderly can be a challenge. Besides the above-described factors, this population is more vulnerable to depression, use of anorexigenic drugs, and dependency on staff for feeding which are described to increase 2 to 3 times the risk of undernutrition [23,25]. Diseases may even interfere with the ingestion or absorption of nutrients, increasing energy requirements. In addition, deficient oral health and feeding difficulty can also worsen nutritional status which by consequence impacts quality of life (QoL) [26–28]. A recent study stressed that the oral health has a limited impact on nutritional status, and, therefore, further studies are needed to support the correlation between these variables [29].

Malnutrition has in fact multifactorial causes, and it is associated with increased susceptibility to infectious diseases due to immunity deficiencies, dehydration, anemia, pressure ulcers, orthostatic hypotension, falls and bone fractures, cognitive deficit, decreased functional capacity and general frailty [30,31]. All of these scenarios boost morbidity and consequently mortality, with greater occurrence of hospital admissions and of their duration, greater use of resources and increased costs.

The prevalence of malnutrition in the elderly is difficult to determine as population cohorts are heterogeneous due to the lack of consensus in terms of methodology and criteria used to define this condition. Overall, it is estimated that malnutrition prevalence overcomes 20% [31]. In institutionalized adults, malnutrition is even higher up to 52% and 85%, depending on the criteria and methodology used in each study [32,33].

Modification of dietary pattern and dietary intakes can potentially improve nutritional status and, thereby, QoL. Diets rich in lipids (mainly saturated fatty acids) and refined carbohydrates have been associated with higher levels of inflammation which, by consequence, may culminate in the development of obesity, cardiovascular disorders, cancer, and diabetes. In turn, vegetable and fruit-based diets have been associated with decreased inflammation, increasing longevity while limiting the prevalence of several chronic diseases [34]. Institutionalized seniors in which undernutrition is frequently detected showed increased inflammation markers and oxidative stress which were correlated with lower cognitive performances [35]. Dietary patterns such as Mediterranean diet or caloric restriction have been associated with increased longevity and less age-associated diseases [36–38].

In addition, oral nutritional supplementation is also a helpful strategy to improve nutritional status, or at least, prevent malnutrition in institutionalized seniors [39]. Upon identification of nutritional deficiencies, specific supplements can be prescribed to prevent/eliminate the referred individual needs. Interestingly, studies showed that nutritional supplementation is often used in conjugation with other nutritional intervention in nursing homes [40,41]. Of note, the use of this strategy is correlated with better QoL and decrease in mortality.

1.3. Methods to screen nutritional status

Nutritional status screening and assessment tools are very helpful in the daily routine to rapidly detect the need, or not, to start an intervention. As in other situations, earlier diagnosis prevents the worst-case scenario and allow a smoother intervention. In addition, early and extended nutrition intervention showed a trend towards improved nutrition status and significantly reduced the duration of hospital stay [42].

There are several tools to assess nutritional risk and status. They vary from questionnaires to anthropometric measurements, the analysis of biochemical parameters, dietary history, clinical history and physical examination or a conjugation of several on a more complex evaluation [43]. However, these tools should be both sensitive and specific, and if possible, predictors of the success of nutritional therapy. In this way, a proper action plan can be implemented. Some basic recommendations should be followed to ensure a good quality of nutritional care in nursing homes. The measurement of weight and height during admission to a nursing home is inevitable. Furthermore, the nutritional status must be assessed in order to be able to provide adequate nutrition.

1.3.1. Anthropometric measures

The core elements for anthropometry are height, weight, body mass index (BMI), body circumferences to assess for adiposity (waist, hip, and limbs), and skinfold thickness [43].

Body weight, height, and the resulting BMI are important parameters which are relatively easy to obtain from patients. However, height may be a difficult-to-measure component of anthropometric assessment in the elderly, as many of them show difficulty in staying in the upright position. Currently, it is possible to estimate height by means of standard formulas by measuring knee height or demi-span [43,44]. More than 30 anthropometric measures are possible as shown in Figure 1.2. The different numbers correspond to a specific measurement either in sitting or standing position [45].

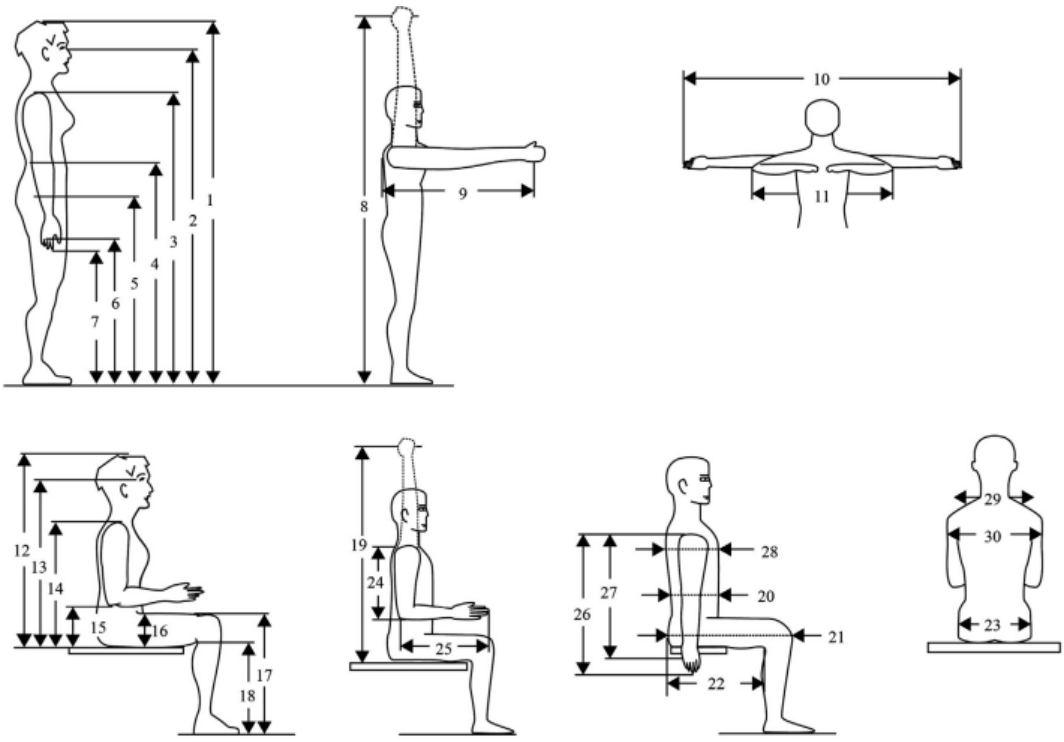

Figure 1.2. Schematic representation of 30 possible anthropometric measurements in standing (1 to 11) and sitting position (12 to 30). Numbers correspond to 1. Stature; 2. Eye height 3. Shoulder height 4. Elbow height 5. Hip height 6. Knuckle height 7. Fingertip height 8. Vertical grip reaches 9. Forward grip reaches 10. Span 11. Elbow span 12. Sitting height 13. Sitting eye height 14. Sitting shoulder height 15. Sitting elbow height 16. Sitting thigh height 17. Sitting knee height. Sitting popliteal height 19. Sitting vertical grip reach 20. Abdominal depth 21. Buttock-knee depth 22. Buttock-popliteal depth 23. Hip breadth 24. Shoulder-elbow length 25. Elbow-fingertip length 26. Upper limb length 27. Shoulder-grip length 28. Chest depth 29. Shoulder breadth biacromial 30. Shoulder breadth bideltoid. Adapted from [45].

The evaluation of body weight, although poses less constrains, should be standardized and preferably be done at the same time of day and with the same amount of light clothing to obtain a reliable weight trend [43]. Standardized weight and height tables are not valid for the elderly as many of them do not include elderly individuals among their samples. More than the total weight, in this age group, the loss or gain of weight was found as a more important risk factor for all-causes of mortality [46]. A natural weight loss occurs after the age of 65. This situation manifests itself by a decrease of only 1% of the usual weight per year. Unintentional weight loss of 5% or more within 6 months to 1 year should be considered relevant and studied carefully [47].

BMI allows to assess body mass in relation to height and is calculated from the weight (in kilograms) divided by the square of height (in meters). This index should be used in association with other indicators, as it does not reflect the distribution of fat normally affected by the aging process. BMI may be also biased by fluid overload and edemas and does not describe body composition. Higher BMI can be calculated in fat individuals and also in very

muscular athletes. Thus, the BMI does not reflect potentially pathological weight loss nor the patient's actual food intake.

In addition, there is a lack of consensus on the definition of appropriate BMI values for seniors. WHO stipulates for adults a "normal" BMI range between 18.9 and 24.9 kg/m^2. However, considering the changes in corporal composition that occur with aging, other values should be used, in order to prevent malnutrition. Lipschitz [48], has suggested a BMI value of 22 and 27 kg/m^2 to underweight and overweight persons, respectively. Supporting this data, a meta-analysis found that mortality was reduced in older adults with BMI values superior to 23.0 kg/m^2 [49]. Similarly, BMI values of 21 or lower should trigger a nutritional intervention as they are related to increased all-cause and cardiovascular mortality in institutionalized elderly patients [50].

Complementary, skinfold thickness may be used to determine total body fat as a one of the easiest and lowest-priced non-invasive methods. By using mathematical formulas, the percentage of body fat can be estimated through the sum of four skin folds: i) biceps (front side of the middle upper arm); ii) triceps skin fold (back side of the middle upper arm); iii) subscapular skinfold (under the lowest point of the shoulder blade); and iv) suprailiac (above the upper bone of the hip).

Tendentially and with aging, fat mass increases and changes its distribution concentrating in the central region of the body. Therefore, waist circumference may be also used to assess under or overweight and cardiovascular risk. It is consensual that this risk increases for values higher than 88 cm in females and 102 cm in males [51].

1.3.2. Questionnaires

Besides the anthropometric measurements of the body, the nutritional status needs to be assessed in further detail and with special methods. Generally, it is recommended to perform nutritional screening to every resident in the first day admission into the nursing home. Nutritional risk screening can rely on the application of rapid and short questionnaires as recommended by the European Society for Clinical Nutrition and Metabolism (ESPEN) [52]. Different contexts require different approaches and so ESPEN proposes the Nutritional Risk Screening 2002 (NRS-2002) for the inpatient setting, the Malnutrition Universal Screening Tool (MUST) for the ambulatory setting and the Mini Nutritional Assessment (MNA) for institutionalized geriatric patients.

MUST was the first of the three questionnaires to be developed to identify malnourished individuals in all care settings. NRS-2002 was derived from it, being a four-questions based questionnaire where if one is positively answered, a detailed follow-up is applied. NRS-2002 has been continuously validated, and has been shown to be very reliable if administered by trained staff [43,53]. However, in MUST, recent food intake is not included, and calculations of the weight loss percentage may be a barrier in busy and overcrowded health care systems [43].

MNA, in contrast with the previous tools, combines both screening of nutritional risk as well as assessment of nutritional status, being most frequently applied in institutionalized geriatric patients. MNA includes important factors for the senior's nutritional status such as loss of appetite, altered sense of taste and smell, loss of thirst, frailty, depression [54]. This tool has been validated in many languages as well as in two formats: complete form and a short-form (MNA-SF). The complete MNA includes eighteen items in four domains while the MNA-SF includes only six items. If in the shorter form, the total score is 11 points or less, the patient is considered at risk of malnutrition or malnourished and the full version should be performed [43]. The maximum score to obtain in MNA is 30 points. The final score allows stratification on the following classes: less than 17 points – malnutrition; between 17 and 23.5 – at risk of malnutrition; and equal to or greater than 24 points – well nourished.

The Subjective Global Assessment (SGA) is also a very used and complete tool which includes information on a medical history (weight loss; dietary intake change; gastrointestinal and functional impairment) and physical examination (loss of subcutaneous fat; muscle wasting; ankle edema, sacral edema, and ascites). This tool has been mainly validated for the nutritional diagnosis of hospitalized clinical and surgical patients. Nevertheless, SGA does not reflect slight changes in nutritional status nor account for biochemical values. Its sensitivity, precision, and reproducibility over time have not been extensively studied in some patient populations [43,55].

1.3.3. Biochemical parameters

Biochemical parameters may be directly affected by variations in nutritional status. Although we must always rely on a combination of analysis, they may provide valuable information about a patient's nutritional status, proof of nutrient deficiency, revealing information about the aetiology of malnutrition and allowing a closer and analytical follow-up nutritional therapy. In addition, some parameters may equally reflect the body inflammatory state that could be

the cause or the effect of malnutrition unveiling information about the severity and activity of the disease or changes in body composition. The most common biochemical parameters evaluated for determination of nutritional status are albumin, pre-albumin, transferrin and the total cholesterol.

Albumin, the most abundant human plasmatic protein, has been considered an appropriate indicator of malnutrition with exception of anorexia and acute illness conditions [43]. Its concentration in the blood depends on the balance between its production, distribution and degradation, being subject to variations during inflammatory processes and liver or kidney failure. Low albumin serum levels (lower than 3.5 g/dl) are normally associated with malnutrition and, therefore, associated with increase in mortality elderly people in the community, in hospital and in nursing homes [56].

Low values of albumin in individuals over the age of 65 years can be attributed to alterations in the synthesis of albumin or even in its distribution across the various body compartments during some illnesses. There is a natural reduction in albumin levels with age, which can be 3 to 8% per decade starting at the 70's. Highest variations should be considered a risk factor and indicator for intervention [57].

Some issues are pointed out in the use of albumin as a parameter for the assessment of nutritional status. On the one hand, albumin levels are influenced by nutritional status, medication taken (such as steroids) and for underlying diseases (such as cirrhosis and nephrotic syndrome). On the other hand, the long half-life (approximately 20 days) may imply a delayed response to variations in dietary-protein intake [43].

The use of serum albumin as a biomarker of nutritional status has been validated while the association of low levels with activity of daily living (ADLs) function has been questioned among elderly without inflammation [58,59]. Nevertheless, higher levels of serum albumin were a protective factor for the decline of ADLs in centenarian persons [60].

In alternative, pre-albumin, a precursor of albumin that is part of a composite protein complex by the retinol transporter protein and by vitamin A has been used. It has a half-life short (48 hours), which makes it a good indicator in evaluating changes in the protein-energy intake. In situations of malnutrition and inflammation the levels are low and are also sensitive to re-nutrition. Pre-albumin levels are affected in cases of zinc deficiency. Pre-albumin values less than 10 mg/dl are synonymous of malnutrition (Table 1.1) [61].

Transferrin has also been used as a marker of nutritional status. It is a protein synthesized in the liver, whose main function is the transport of serum iron. In relation to albumin, it has a

shorter half-life (about 10 days), being more sensitive to changes in the protein synthesis process. Iron deficiency and infection directly interfere with the hepatic synthesis of transferrin and may change its levels (Table 1.1) [61].

Transferrin reference values are between 160 and 360 mg/dl. Nevertheless, transferrin serum levels have been found to be unreliable in the assessment of mild malnutrition and of fat-free mass in a group of elderly Italian patients [62].

Other biomarkers than visceral proteins such as cholesterol or urinary creatinine have been used as laboratory markers of malnutrition. Still, their role in diagnosing or monitoring malnutrition is controversial, as more recent studies have shown [61].

Table 1.1. Characteristics of serum proteins used as nutritional biomarkers [61].

Protein	Molecular Weight (Da)	Half-Life (days)	Reference Range (g/dL)
Albumin	65 000	20	3.30 – 4.80
Pre-albumin	54 980	2	16 – 35
Transferrin	76 000	10	0.16 – 0.36

1.3.4. Clinical Evaluation

Clinical evaluation is a subjective and retrospective description of the patient's condition. Some important aspects for the diagnosis of malnutrition, such as: chronic diseases (diabetes, insufficiency renal, cardiac pathology, etc.); gastrointestinal disorders; usual medication; weight changes and ability to perform ADLs can be an interesting starting point of the nutritional assessment [43].

Physical examination can be included in the clinical evaluation supporting a more complete nutritional assessment. The main clinical signs of malnutrition and nutritional deficiencies occur at different levels in different body regions (Table 1.2) [63]. Some clinical signs are specific of disease or nutrient deficiency. Others are non-specific and need further tests to elucidate their origin [43].

To complement clinical evaluation with dietary and eating habits and behaviors is also fundamental to best under nutritional needs and status of the seniors. Knowing current and past eating habits including food choices based on their tastes, the number and type of meals,

eating, chewing, and swallowing difficulties will help to adjust further needed strategies to prevent or treat malnutrition [43,63].

Table 1.2. Clinical Signs of nutritional deficiencies. Adapted from [63].

Sign/Symptom	Nutrient Deficiency
Skin	
Dry Scaly skin	Zinc/Essential fatty acids
Follicular hyperkeratosis	Vitamin A and C
Petechiae	Vitamin C and K
Photosensitive dermatitis	Niacin
Poor wound healing	Zinc, Vitamin C
Scrotal dermatitis	Riboflavin
Nails	
Transverse depigmentation	Albumin
Spooned	Iron
Hair	
Thin/depigmented	Protein
Easy pick ability	Protein, zinc
Eyes	
Night blindness	Zinc, Vitamin A
Conjunctival inflammation	Riboflavin
Keratomalacia	Vitamin A
Mouth	
Bleeding gums	Vitamin C, riboflavin
Glossitis	Niacin, pyridoxine, riboflavin
Atrophic papillae	Iron
Hypogeusia	Zinc, Vitamin A
Neurological	
Ataxia	Vitamin B12
Tetany	Calcium, Magnesium
Paresthesia	Thiamine, Vitamin B12
Dementia	Vitamin B12, niacin
Hyporeflexia	Thiamine

1.4. Nutritional recommendations for older adults

Older adults are a diverse population with different aging rates, making them vulnerable to nutritional inadequacies and hampering the setting of uniform nutritional recommendation [64]. Food intake is typically decreased in older adults and energy requirements are lower. Therefore, the challenge for older people is to meet the same nutrient needs but consuming fewer calories.

The aging process is associated with significant inability to control food intake and loss of appetite which imbalances the equilibrium between dietary needs and real intakes. Although the mechanisms associated to anorexia of aging are not fully clarified, two main general mechanisms are described for the development of the age-related appetite decline: (1) reduced drive to eat (hunger) resulting from lower energy requirements, and (2) more rapidly acting or more potent inhibitory satiety signals [65]. A poor nutritional status and low energy intake may affect both cognitive and functional ability, compromising general health [66]. This process may be worsened by institutionalization. A cross study performed in Finland revealed that a high percentage of residents in nursing homes consume less fiber, vitamin E, vitamin D, and folic acid than the recommended values [67]. In comparison with elders living in the community, institutionalized individuals display different dietary patterns. Nursing home residents consume less proteins, more non milk extrinsic sugars and have reduced micronutrient intakes when compared with home-dwelling individuals [68,69]. Furthermore, institutionalized seniors ingested less food containing zinc and iodine whereas the intake of iron, selenium and copper did not differ significantly [70].

The nutritional recommendations established for older adults have been based on the needs of healthy individuals. There are numerous nutritional recommendations, according to the different organizations. In Europe, *European Food Safety Authority* (EFSA) set average dietary reference intake values (DRV) as nutrient reference values to guide professionals on the amount of a nutrient needed to maintain health in an otherwise healthy individual or group of people [71]. Table 1.3, presents the DRV values for the different nutrients (macronutrients, micronutrients and fluid intake) according to gender and age group above 60 years old [71,72].

Older adults are a very heterogeneous group regarding activity, functionality and health status. Given this heterogeneity, regular weight measurements, physical capacity and force may help to determine whether the amount and composition of diet is appropriate for a given person. Individual differences in energy needs and requirements are possible.

In this thesis, reference intake ranges were used for macronutrients, whereas average requirements, adequate intake or tolerable upper intake level were used for micronutrients, depending on which reference value is available [71,72]. Additional cut-offs (1.0 and 1.2 g/kg) were studied for protein per kg of body weight, based on recent clinical guidelines for older adults [73].

Table 1.3. Dietary Reference Intake Values for older adults [71,72].

	Dietary Reference Values			
	Age 60 - 69		**Age 70+**	
	Male	**Female**	**Male**	**Female**
Energy (kcal)	2006.2	1624.0	1982.3	1624.0
Protein (g)	54	41	54	41
Fat (g)	66	54	66	54
Carbohydrates (g)	100	100	100	100
Total fiber (g)	25	25	25	25
Water (ml) [drinking/mineral water and from food moisture]	2500	2000	2500	2000
Vitamin A (µg)	750	650	750	650
Vitamin C (mg)	110	95	110	95
Vitamin D (µg)	15	15	15	15
Vitamin E (mg)	13	11	13	11
Vitamin B1 (mg)	1.0	0.8	1.0	0.8
Vitamin B2 (mg)	1.6	1.6	1.6	1.6
Vitamin B3 (mg)	15.4	12.5	15.2	12.3
Vitamin B6 (mg)	1.7	1.6	1.7	1.6
Vitamin B12 (µg)	4	4	4	4
Folic Acid (µg)	320	320	320	320
Sodium (mg)	2000	2000	2000	2000
Potassium (mg)	3500	3500	3500	3500
Calcium (mg)	1000	1000	1000	1000
Phosphorus (mg)	550	550	550	550
Magnesium (mg)	350	300	350	300
Iron (mg)	11	11	11	11
Zinc (mg)	11.7	9.3	11.7	9.3
Selenium (µg)	70	70	70	70
Iodine (µg)	150	150	150	150

1.4.1. Energy

The perception of energy requirements in older adults is essential to avoid undernutrition or overnutrition and for the targeted nutritional support not only in healthy elderly people but also in those who are malnourished, frail, sarcopenic or affected by chronic diseases [74].

Energy requirements are routinely calculated by multiplying estimated or measured resting energy expenditure (REE) plus physical activity and disease coefficients. Energy needs decline gradually with aging due to a decrease in both REE and physical activity level (PAL) [73].

The PAL is a measure for the physical activity as stated below [75]:

- PAL 1.6 mainly walking or standing activity (e.g. patient with Alzheimer's disease)
- PAL 1.4 sedentary activity, temporarily walking or standing
- PAL 1.2 only sedentary activity or bed-ridden

The general basal metabolic rates for people aged 65 and older that are multiplied with the PAL are for men 5.9 MJ/d (1 410 kcal/d) and for women 4.9 MJ/d (1 170 kcal/d) [71,72]. The reference values for the total energy needs are for men 2 300 kcal/d and for women 1 800 kcal/d [76].

A rule-of-thumb exists for calculating the caloric needs of patients [77]:

- immobile: ca. 20-25 kcal/kg BW/day
- mobile: ca. 25-35 kcal/kg BW/day

The individual energy need is calculated with the Harris-Benedict formula. Although this formula is poor in the prediction of basal metabolic rate at group level, it works quite well for individual level [78]:

- Women: Basal metabolic rate [kcal/24h] = 665.1 + (9.56 x body weight [kg]) + (1.85 x body height [cm]) - (4.67 x age [years])
- Men: Basal metabolic rate [kcal/24h] = 66.47 + (13.75 x body weight [kg]) + (5 x body height [cm]) - (6.76 x age [years])

1.4.2. Macronutrients

No significant changes in macronutrients requirements occur throughout the human life cycle. Nevertheless, an adequate protein intake should be taken in consideration to support

healing, skin integrity, immunity, recovery from illness, muscle wasting, and to optimize bone mass, namely in the elderly [64,79].

The current protein reference nutrient intake is 0.8g protein/kg body weight in healthy adults of all ages [79]. The need to increase protein intake is controversial among authors. However, emerging evidence-based studies have argued that an increased protein intake may be beneficial to fulfill the needs of vulnerable older adults, particularly those with chronic diseases [80,81].

Similarly, and to balance macronutrient energy source, sufficient carbohydrates should be ingested such as complex carbohydrates [64]. In conjugation with water, this class of macronutrient can contribute to alleviate constipation, which is a common problem in older adults, especially those who are physically inactive and take multiple medications.

For the lipids, the major concerns are related to dietary excess that is associated with refined carbohydrates that may lead to the increase of obesity and the incidence of chronic diseases.

1.4.3. Micronutrients

Older people may require larger amounts of micronutrients. However, micronutrients can be easily obtained by a healthy well-balanced diet which contains a variety of foods from the major food groups [64].

Calcium is an integral component of the skeleton and also acts as an essential intracellular messenger in cells and tissues. If the dietary supply of calcium is insufficient to meet physiological requirements, this could cause a reduction in bone mass, which leads to osteopenia and osteoporosis with an associated increase risk of fracture. The mean value in which calcium intake equals excretion (considering dermal losses of calcium) results in an AR of 750mg/day and a PRI of 950mg/day. Calcium bioavailability differs according to sources and foods or interactions with other nutrients or differences depending on the physiological situations, like menopause [82]. So, we considered the values proposed by Scientific Committee of the Spanish Agency for Food Safety and Nutrition (1000mg/day) [82]. Vitamin D deficiency leads to impaired mineralization of bone (due to an inefficient absorption of dietary calcium and phosphorus). Vitamin D might be present in the organism by three ways: from the diet, through the skin from sunlight, and from supplements. For Vitamin D, the defined adequate intakes were 15µg/day instead of ARs or PRIs [71]. Vitamin B6 recommendations rise to 1.7 and 1.6 milligrams per day for older men and women,

respectively. Vitamin B6, vitamin B9 and vitamin B12 are very important to help lower levels of homocysteine and protect against cardiovascular disease [83].

Food supplementation may be considered in special cases where gastrointestinal diseases reduce nutrient bioavailability. Specifically, in case of Vitamin B12, a generalized recommendation for consuming foods fortified with vitamin B12 or a food supplement containing vitamin B12 may be beneficial as the production of stomach acid usually decrease, hampering Vitamin B12 absorption [83].

1.4.4. Fluid's intake

The decline of kidney function, the use of multiple medications in special diuretics and subsequent consequences of dehydration including constipation, confusion, bladder infections, functional decline, falls, or stroke put particular focus on water intake [64]. Inadequate hydration in the elderly is associated with increased morbidity and mortality [84] and can also affect saliva production, which is essential for maintaining the health of the mouth and for proper chewing of food and its subsequent absorption [64].

Adequate total water intakes for females would have to be 2.0 L/day and for males 2.5 L/day. So, it's important to encouraging elderly to consume water even without feeling thirsty [71,73]. In fact, increased fluid intake such as tea was associated with better performance on focused and sustained tasks as well as increased psychomotor performance [85,86].

1.5. Dietary assessment tools

There are different techniques to quantify foods eaten by the elderly. This assessment can be performed through retrospective or prospective data collection or regarding the individual's food intake. In this way, dietary intake can be quantified and related to specific individual recommendations.

According to intellectual capacity of individuals, availability of qualified personnel and other factors, different methods can be implemented to access dietary intake.

1.5.1. Daily Food Record/Food Diary

Food diary consists of the regular register of food intake during the day. At the end of the desired registration period (usually between 3 to 7 days) the individual's nutritional intake is calculated by establishing average consumption.

1.5.2. 24-hour dietary recall

This is a retrospective method of assessing food and beverages intake, in which the individual draws up a list of all foods consumed in the 24 previous hours. The interview is conducted in two ways: "starting to recall from the beginning of the recalling day" or "starting with the current day and working backward" and in general requires approximately 15 to 20 minutes depending on the types and variety of the food that was consumed [87].

The list of foods is then analyzed by the specialist responsible for collecting the information. The main limitation of this tool is the individual's inability to precisely remember the type and amount of food eaten; difficulty in determining whether the day chosen for recording is representative of intake of usual food; the tendency to overestimate low intakes and underestimating higher food intakes [88].

1.5.3. Food Frequency Questionnaire

The food frequency questionnaire is a retrospective review of the frequency of food intake relatively easy to apply and cheap [89]. It allows us to estimate the specific macro and micronutrient an individual consumes during a specific period of time, usually one day to several months. Food frequency questionnaires are largely dependent on the individual's ability to memorize and quantify the particular food or food group consumed [87]. Deviation from reality intensified when the food list of questionnaire increases.

1.6. Functional capacity and cognitive status

Functional and cognitive abilities often decline with aging. Functional ability is defined as the potential of elderly people to decide and act independently in their daily living while cognition involves the entire sphere of mental functioning and includes the ability to feel, think, perceive, remember, reason, form complex structures of thought, and to produce responses to external demands and stimuli [90].

Regular physical activity has positive effects on systems: musculoskeletal, cardiovascular, respiratory and endocrine; beyond directly interfering with well-being and reducing morbidity and mortality [91]. With advancing age, individuals tend to decrease physical activity and consequently the energy expenditure which contributes to the positive energy balance (with the subsequent increase in weight gain) and for negative alterations manifested in body composition (decrease in lean mass and increase in fat mass) with atrophy of the skeletal muscular system. This imbalance may result in sarcopenic obesity which has functional consequences such as disability and illness [92].

Age-associated loss of muscle mass, known as sarcopenia, is the direct cause of the decrease in muscle strength, being the main cause of disability. Moreover, decreased muscle power and strength become determinant aspects of the ability to walk. The high prevalence of falls among institutionalized elderly may be directly related with the decrease in muscle strength [93].

Mental health and basic cognitive function are relevant capacities of the elderly person and have become a focus of public health research, namely its preservation or just to delay the normal decline [94]. Previous data has shown that higher educational level and active social engagement are protective factors for cognitive function [94]. In contrast, a recent longitudinal study showed that neuropsychiatric symptoms – including depression – are risk factors or clinical indicators of preclinical dementia syndrome increasing to some extent the risk of cognitive impairment [95].

Both cognitive and functional capacities are interconnected. A systematic review pointed out a strong but one-sided association between cognitive and functional impairment [96]. Deficits caused by cognitive decline led to disability, with a reduction and/or loss of abilities to perform activities of daily life. However, functional impairment does not necessarily result in deterioration of cognitive functions.

1.7. Polypharmacy and potentially inappropriate medication (PIM)

Polypharmacy is defined as the use of multiple medications by a patient, being that there is no standardized minimum threshold for the number of medicines [97]. Despite this, in our study we considered that polypharmacy was divided into minor (2 to 4 daily medicines) and major (5 or more daily medicines). Polypharmacy is a common and important problem related to the use of drugs that have been increasing due to multimorbidity in the elderly [97].

Polymedication is common in elderly people because of the various coexisting health problems, which in turn take multiple drugs, as one or more drugs can be used to treat each clinical situation.

It is imperative that medicines for the elderly are properly prescribed, available, and affordable. However, polypharmacy is verified in 20 to 30% of older adults taking more than four medications. On average, nursing home residents take more than eight drugs per day [98]. Besides increasing health care costs, polypharmacy increases the risk of adverse drug events, drug interaction and the use of Potentially Inappropriate Medications (PIMs) [99]. Older people whose physiological changes related to aging can cause drug pharmacokinetics and pharmacodynamics changes, with particular reference to hepatic elimination and renal excretion, are more susceptible to these effects [100]. Gurwitz *et al.* estimated that 51% of the found adverse drug events were presumably preventable [101]. Furthermore, in this age group, polypharmacy is also often associated with physical dysfunction and cognitive decline [102].

The management of polymedication should, on one hand, to optimize patients care with multimorbidity and, on the other hand, to maximize the benefits and reducing the risks of potentially inappropriate medication [103,104]. Thus, the involvement of a multidisciplinary team composed by doctors, pharmacists, nurses and other health professionals should make the complex decision, according the best standards of evidence-based, in order to eliminating/reducing PIMs. For instance, the Beers Criteria has been one of the most used methods to assess PIM use [100]. These guidelines are frequently revised by the American Geriatric Society, listing the medicines that should be typically avoided by older adults in normal conditions or under specific situations, such as in certain diseases or conditions [105].

Chapter 2 | The role of nutritional status on polypharmacy, cognition and functional capacity of institutionalized elderly: A systematic review

Adapted from:

Caçador, C.; Teixeira-Lemos, E.; Martins, S.O.; Ramos, F. The Role of Nutritional Status on Polypharmacy, Cognition, and Functional Capacity of Institutionalized Elderly: A Systematic Review. *Nutrients* 2021, *13*, 3477. https://doi.org/10.3390/nu13103477

2.1. Introduction

Nutritional status is an important condition that deeply affects the general health of the elderly [63,106]. Despite the recommended intakes of most nutrients do not or only minimally change with age, decreased olfaction, taste and vision combined with physiological changes that promote insufficient ingestion and poor absorption of essential nutrients may demand a compensatory nutrients intake as age increases [18,107].

While the worldwide population is increasingly aging and the number and proportion of elderly in the overall population rises, older adults' institutionalization is becoming an expressive reality. This trend is driven by the increased demand for care of the elderly, whose families may not have financial or structural resources to support [11,12]. Institutionalization process may radically affect the daily lives of older adults, namely in terms of nutrition, cognition and level of functioning [13].

Among old, institutionalized subjects, alterations in nutritional status are frequently detected. The number of malnourished institutionalized elders is significant, ranging from 20% to 60%, depending on the criteria and methodology [23,25,33,108]. Moreover, this population is more vulnerable to depression, the use of anorexigenic drugs and dependence on staff for feeding, which have been described as a 2- to 3-fold increased risk of undernutrition [23,25].

Diseases which affect more than 80% of people over 85 years old may even increase drug consumption and the risk of polypharmacy [109,110]. Older people often present physiological changes related to aging that cause drug pharmacokinetics and pharmacodynamics changes. Hepatic elimination and renal excretion are particularly affected, interfering with the ingestion or absorption of nutrients, thereby increasing energy requirements [100]. Institutionalization presents an incremented risk factor over age for polypharmacy. Twenty to 30% of older adults take more than four medications, whereas nursing home senior residents take more than eight drugs per day. Moreover, polypharmacy was observed to have a significant association with physical function, nutrition, and depression in the elderly [111,112].

Deficits caused by cognitive decline can lead to disability, thereby reducing and/or losing the ability to perform activities of daily living. Regular exercise and an active lifestyle were associated with a decreased risk of dementia [113–116]. Furthermore, functional, and cognitive abilities and poorer nutritional status are reported to be very closely linked to each other. Malnourished older adults or even at risk of malnutrition presented lower cognitive abilities than those with a normal nutritional status [117,118].

In face of these numbers and facts, a relationship between nutritional status, polypharmacy, cognition and functional ability in elders seems to be at first sight logical, however concrete

data are scarce and lack consistency in terms of both used tools and well-defined population characteristics. The number of institutionalized seniors has increased worldwide and only now the first repercussions of this phenomena are being reported [119]. The association between nutritional status with cognition, functional ability and polypharmacy in institutionalized elderly remains poorly characterized [120,121]. In this systematic review, we aimed to present a comprehensive overview of the peer-reviewed studies conducted specifically on nursing homes residents where nutritional status was correlated with polypharmacy, cognitive decline, and functional capacity. Nutritional patterns and needs are moldable factors at the individual level and therefore this research may help to consolidate the relevance of maintenance of nutritional status to preserve other health domains of the elderly that are institutionalized.

2.2. Methodology

This systematic review was performed according to the relevant point of the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-analyses) guidelines [122,123].

2.2.1. Eligibility criteria

Inclusion criteria

Peer-reviewed studies describing interventional, observational, or randomized controlled trials were included. Inclusion criteria were established according to the above-described PICO strategy.

Population: older adults over 65 years of age, living in nursing homes. No specific health condition was used for exclusion.

Intervention: All forms of nutritional patterns

Comparator/Control: All studies were included irrespective of the presence or absence of comparator or control groups.

Outcomes: any correlation between nutritional status with at least one of the other features (polypharmacy, cognitive function, and functional capacity). Notably, studies that assessed malnutrition by assessment tools (e.g., MNA) were included. There were no restrictions placed at the time of follow-up.

Exclusion criteria

Studies published in a language other than English or Portuguese.

Publications comprising editorials, comments, letters to the editor, guidelines, theses, books and scientific meeting abstracts, literature reviews or case reports.

Studies conducted on participants with a mean age below 65 years and in a different setting than nursing homes.

Studies that did not report any results for an outcome measure of nutritional status.

Publications without description of the impact of nutritional status outcomes on polypharmacy, cognition, or functional ability.

Studies which used oral supplementation to preserve nutritional status.

2.2.2. Search strategy

In February 2021, an independent researcher (C.C.) searched the PubMed and Web of Science databases without language restrictions in the past ten years (since 2011). The author (C.C.) also reviewed the reference lists from the review articles reported in the PubMed and Web of Science searches to identify possible additional articles for inclusion. Cochrane library was also consulted however no additional studies were found. A combination of the following search terms was used: institutionalization AND Nutritional status AND Cognition, institutionalization AND Nutritional status AND functional capacity, institutionalization AND Nutritional status AND polypharmacy.

2.2.3. Selection process

All search results were exported to Microsoft Office™ Excel, using Mendeley Desktop® software.

2.2.4. Data extraction

The following data were extracted from each study (CC) and validated by the second author (E. T-L.), elaborating a systematic database:

- Title, authors and main aim of the intervention (cognitive/functional dependence/polypharmacy);
- Demographic information of the participants: setting, country, sample size, sex, age;
- Study characteristics: nature, aim;

- Statistical analysis and outcomes;
- Tools/methods used to collect data.

Outcome measures in the domains of nutritional status were sought independently or in combination with cases of decline in cognitive function and functional abilities. Differences in the criteria of assessment tools used for nutritional status, cognitive function and functional abilities were recorded and discussed.

Results from the initial search were evaluated separately by the two review authors (CC and ETL) according to the inclusion criteria. First, the results were screened by reading the article titles and excluding articles that were not relevant according to the inclusion criteria. Next, the study abstracts were evaluated, and non-relevant articles were excluded. Finally, the full-text articles selected by the two reviewers were collected and assessed for their relevance relative to the inclusion criteria. Any disagreements regarding the eligibility of studies were reconciled at the final step by discussion and consensus.

2.2.5. Risk of Bias (RoB) assessment and overall quality

The methodological quality of the studies was assessed by two independent reviewers (C.C. and E. T-L.) based on different domains, such as study participation, confounding variables, measures of risk factors, analysis, and reporting. The risk of bias and the quality of each study were discussed between the two researchers until a consensus was reached.

Evidence and methodological quality were assessed according to the Quality in Prognosis Studies (QUIPS) tool [124,125]. To rate the strength of study outcomes, the following six domains were considered: 1) Study Participation, 2) Study Attrition, 3) Prognostic Factor Measurement, 4) Outcome Measurement, 5) Study Confounding and 6) Statistical Analysis and Reporting. Overall domain ratings were based on the number of assessment criteria in QUIPS met by each study in combination with their associated risk factors: if the majority of criteria were met with little or no risk of bias, a '++' rating was assigned; if most criteria were met, but some flaws in the study posed an associated risk of bias, then a rating of a '+' was assigned, while the domains in which most of the criteria were not met with significant flaws in key aspects of the study were given a rating of '-'.

Summarizing RoB is usually not linear, as there are no explicit criteria in the literature that pinpoint how to classify the overall RoB of a paper [117]. After continuous discussions from the authors, and after considering Study Participation, Prognostic Factor Measurement and Outcome Measurement as critical to our review of the study, the following categorization was

decided: (i) studies with a '++' rating in at least two of the aforementioned critical domains were defined as low RoB; (ii) studies with a '-' rating in any of the critical domains or with a '+' rating in four or more domains were defined as high RoB and (iii) all papers in between were classified as having moderate RoB. No article was excluded based on this assessment.

2.3. Results

2.3.1. *Study Selection and Literature review*

The rationale for identification, screening, eligibility, and inclusion of articles is shown in Figure 2.1.

The search recorded 186 non duplicated references, with 95 classified as potentially relevant after checking the titles and abstracts. After the screening of the full texts, 87 articles were excluded because they did not meet the inclusion criteria namely the evaluation of nutritional status or its influence on cognitive or functional features. Ultimately, only 8 original publications were selected and included in the review (Figure 2.1).

Table 2.1 displays a descriptive review of the included articles (n=8), summarizing the impact of nutritional status on cognitive capacity and functional ability [25,85,126–131]. No studies were found to be associated with alterations in nutritional status and prevention of polypharmacy.

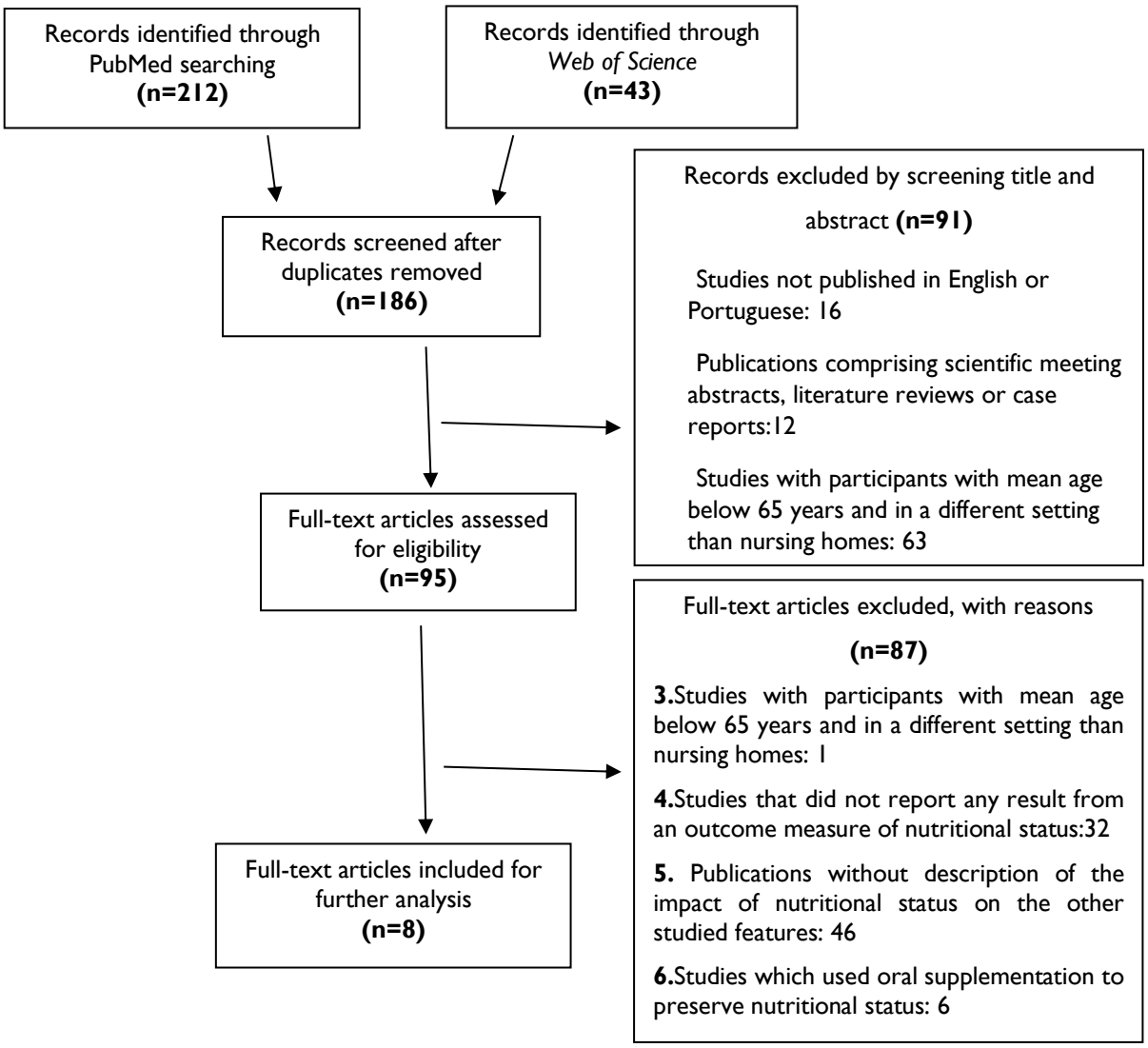

Figure 2.1. PRISMA flow diagram. Exclusion criteria were: 1) Studies published in another language than English or Portuguese; 2) Publications comprising scientific meeting abstracts, literature reviews or case reports; 3) Studies with participants with mean age below 65 years and in a different setting than nursing homes; 4) Studies that did not report any result from an outcome measure of nutritional status, 5) Publications without description of the impact of nutritional status outcomes in polypharmacy, cognition, or functional ability and 6) studied which evaluate oral supplementation efficacy.

2.3.1. Literature review

Table 2.1 displays a descriptive review of the included articles (n=8), summarizing the impact of nutritional status on cognitive capacity and functional ability, respectively. No studies were found to be associated with alterations in nutritional status and prevention of polypharmacy.

Table 2.1. Description of Reviewed Studies on the Impact of Nutritional Status on Cognitive Function and functional capacity in Institutionalized Seniors.

Author/Year	Study Design	Participants	Outcome Measurements				Main Results
			Nutritional Status	Cognitive Function	Functional Capacity	Other	
Li *et al.,* 2013[126]	Cross-sectional study	306 (Mean age: 80.6±7.1, 47.7% female)	MNA	SPMSQ	Modified BI	NA	Both ADLs and depressive symptoms were significantly associated with nutritional status ($p<0.001$)
Mendonca *et al.,* 2017[127]	Prospective longitudinal study **Follow-up:** 1.5, 3 and 5 years	765 (Age over 85 years old, 66.0% female)	BMI and Biochemical parameters: Baseline RBC folate, plasma vitamin B12, and tHcy concentrations	MMSE	NA		Higher RBC folate and lower tHcy concentration measured at baseline were associated with better global cognition as measured by the MMSE ($p<0.001$).
Donini *et al*., 2020[25]	Cross-sectional study	246 (Mean age: 80.4±10.5, 66.7% females)	Height, weight, and calf and mid-arm circumference measurements Modified MNA	MMSE,	Katz Scale SPPB	Disease-related multi-morbidity: Cumulative Illness Rating Scale	Physical performance, depression and cognitive function are significantly and positively associated with the M-MNA total score ($p<0.001$).
Pedrero-Chamizo *et al.,* 2020[128]	Prospective longitudinal study Follow-up: 1 year	60 (Mean age: 80.6±9.9, 68.3% females)	Biochemical parameters: Serum cobalamin, Total-cholesterol, HDL-cholesterol, LDL-cholesterol, triglycerides, apolipoprotein A1 (ApoA), apolipoprotein B (ApoB), lipoprotein A (LpA), glucose, albumin, and creatinine	MMSE	HGS, Upper body strength (Arm curl test) and Lower body strength (30-s chair stand test)	NA	MMSE scores showed a significant positive correlation with sCbl, HDL-cholesterol, ApoA, and albumin ($p<0.05$). Significant negative correlations with HGS were observed for RBC folate, total-cholesterol, LDL-cholesterol, and triglycerides. Biomarkers, except HDL-cholesterol, lost their association with HGS when observed as covariates.
Assis *et al*., 2020[129]	Cross-sectional study	95 (Mean age: 73.3±12.5, 69.8% female)	MNA Anthropometric values: weight and height (to calculate body mass index - BMI), mid-upper arm circumference (AC), calf	MMSE	ADL	NA	The participants with higher scores in MNA (normal and at risk of malnutrition) had higher scores in MMSE compared to malnourished ones ($p<0.001$). Participants that practiced more AADLs (9 to 13

			circumference (CC), waist circumference (WC), and hip circumference (HC)				activities) had higher MMSE scores (p=0.031) compared to those that practiced fewer activities.
Cereda *et al*., 2013[130]	Multicenter prospective cohort study Follow-up: 5 years	346 (Mean age: 85.7±9.1, 74.6% female)	GNRI	NA	BI	NA	Functional status was significantly associated with nutritional risk by GNRI (P<0·001).
Pereira *et al*., 2014[131]	Cross-sectional study	359 (Mean age: 79.5±9.3, 72.7% female)	MNA	MMSE GDS	Scale Of ADL	Presence of comorbidity (hypertension, diabetes mellitus and dyslipidemia)	Nutritional status was associated with dyslipidemia (p=0.029), cognitive capacity (p=0.006), the suspicion of depression (p=0.048) and functional capacity for ADLs (p<0.001)
Serrano-Urrea& García-Meseguer, 2014[85]	Cross-sectional study	895 (Mean age: 82.3±7.1, 58.4% female)	MNA	NA	BI	NA	MNA and the BI scores were positively associated (r=0.375; p<0.001)

ADL: Activity of Daily Living; **BI:** Barthel Index; **BMI:** Body Mass Index; **GDS**: Global Deterioration Scale; **GNRI:** geriatric nutritional risk index; **HGS**: Hand Grip Strength; **MMSE**: Mini-Mental State Examination **MNA:** Mini Nutritional Assessment **SPMSQ:** Short Portable Mental Status Questionnaire; **SPPB:** Short Physical Performance Battery.

2.3.1. Quality assessment

More than of the studies were rated as having a low RoB (n=5) based on the QUIPS tool in combination with the authors' predefined criteria. These papers had strong study participation through methodologically validated tools in combination with clear descriptions of potential confounders and outcome measurements. Three studies were rated as having a "high" RoB (Table 2.2) [128,130,131]. The limitations identified in these studies were commonly considerable data loss and/or poor sampling frame and recruitment.

Table 2.2. Overall Risk of Bias

Study	1	2	3	4	5	6	Overall RoB Rating
Donini *et al.*[8]	++	+	++	++	-	+	Low
Li *et al.*[31]	++	+	++	++	-	+	Low
Mendonca *et al.*[32]	++	+	++	++	+	+	Low
Pedrero-Chamizo *et al.*, 2020[33]	+	+	++	++	+	+	High
Assis *et al.*, 2020[34]	++	+	++	++	-	+	Low
Cerda *et al.*, 2013[35]	+	-	+	+	+	+	High
Pereira *et al.*, 2014[36]	+	-	+	+	+	+	High
Serrano-Urrea& García-Meseguer, 2014[37]	++	+	++	++	-	+	Low

1 = Study Participation; 2 = Study Attrition; 3 = Prognosis Factor Measurement; 4 = Outcome Measurement; 5 = Study Confounding; 6 = Statistical Analysis and Reporting; '++' corresponds to low RoB, '+' was assigned to moderate RoB studies and '-'was given to high RoB.

2.3.1. Participants and follow-up

Table 2.1 shows the number of participants assessed in each study included in this review as well as the mean age and the representativeness of females in the study samples. The final sample ranged from 23 to 2919. With the exception of Li *et al.*, all of the samples included more than 60% of females. Follow-up periods varied considerably – from 1 week to 5 years.

2.3.2. Characteristics of studies and outcomes measures

Table 2.1 shows the methods used as outcome measures in the included papers. Five studies [25,85,126,129,131] used MNA (short or long form) to evaluate nutritional status which used a standard <17 points (long form) or <7 points (short form) as a measure of nutritional status.

One study used BMI (kg/m^2) to measure nutritional status [127], one used biochemical parameter and another one used the geriatric nutritional risk index (GNRI) [130].

Cognitive function was measured in six studies [25,85,126,128,129,131]. The types of assessment differed slightly, with negligible variations in the cut-off value for the same type of assessment. Five studies [25,127–131] used the well-known and rapid Mini-Mental State Examination (MMSE). Two studies [128,129] defined <24 points as cognitive impairment. One study used <19 points as a measure of cognitive impairment [25], while another study [126] used the Short Portable Mental Status Questionnaire (SPMSQ) to define scores between 8 and 10 as intact cognitive functions.

Seven studies [25,85,126,128–131] assessed functional capacity. Half of the studies (n=4) [85,126,128,131] used the Barthel Index (BI), a tool developed to cover all aspects of self-care dependence in activities of daily living, where a score of 100 indicates functional independence. Notably, every study that used the BI reported cut-off values. Two studies measured the level of dependence on activities of daily living (ADL) [129,131] while one study [25] focused on ADL using the Katz Scale and assessed physical performance through the Short Physical Performance Battery (SPPB). One study assessed handgrip strength and used arm curl/lift as a performance test [128].

In all evaluated studies, a statistically significant association between cognition or functional capacity and nutritional status was pointed out. Serrano-Urrea & García-Meseguer reported a positive association between MNA and BI scores ($r=0.375$; $p<0.001$) [85] and Cereda *et al.* concluded a significant association between GNRI and functional status [130].

Li *et al.* [126] found that both ADLs and depressive symptoms were significantly associated with nutritional status ($p<0.001$). Similarly, Assis *et al.* [129] described that higher MNA scores (normal and at risk of malnutrition, MNA >17) had higher scores in MMSE compared to malnourished ones ($p<0.001$) and that more active participants who practiced between 9 to 13 ADLs had higher MMSE scores ($p=0.031$) compared to those that practiced fewer activities. Donini *et al.* [25] validated the already reported results showing that physical performance, depression and cognitive function were significantly and positively associated with the MNA total score ($p<0.001$). Pereira *et al.* [131] also associated nutritional status with cognitive capacity ($p=0.006$), the suspicion of depression ($p=0.048$) and functional capacity for ADLs ($p<0.001$) as well as with dyslipidemia ($p=0.029$).

Different blood biochemical parameters used to determine nutritional status were correlated with MMSE scores. Higher RBC folate and lower tHcy concentration were associated with

better global cognition as measured by the MMSE ($p<0.001$) [127] as well as Cbl, HDL-cholesterol, ApoA, and albumin ($p<0.05$) [128].

2.4. Discussion

Eight studies were found relating nutritional status with at least one of the following domains: cognition or functional capacity and a clear relationship between nutritional status and cognitive and functional abilities was found in institutionalized seniors.

According to the studies, a close relationship exists between nutritional and functional domains in long-term care residents [130,131]. Impairments in functional ability and nutritional status often occur with overlapping outcomes such as muscle loss, weakness, and frailty [132]. The results of this review found that there were slight variations in functional abilities assessment. The BI and the Katz Scale were the most commonly used tools to assess ADL in older adults. These two validated tools are very comprehensive and can provide useful insights into a patient's functional capacity. The choice to use one of these tools is not often linear and should be made based on a case-by-case assessment. Notwithstanding, the Katz scale was developed to be recorded over a period of time. As such, it may be more suitable for long-term care settings. In addition, the approach to measuring functional dependence could benefit from a multifaceted strategy. Findings from this review suggest that anthropometric measures such as weight, height, waist circumference, and body mass index (BMI) may provide a more accurate understanding of functional status in older adults when combined with ADL assessment.

Different studies have also shown that nutritional status affects cognition. Normal levels of folate, total homocysteine, serum cobalamin, HDL-cholesterol, and triglyceride levels were important biomarkers for cognition, however they were not identified as predictive factors for cognitive decline [127,129]. Of note, Pedrero-Chamizo *et al* also correlated these biomarkers with functional performance [128].

Depressive symptoms, and cognitive symptoms associated, are often reported in the institutionalized elderly. This fact is extremely relevant when evaluating institutionalized elderly. In addition to presenting a higher risk of malnutrition, the prevalence of cognitive deficits and other neurological disorders is high among home care older adults. The findings of this review regarding the association between nutritional status and depression and subsequent cognitive performance are somewhat limited and should therefore be interpreted with caution. If preventive strategies fail to diagnose or treat depressive symptoms, specific dietary changes may be of immeasurable value. Nevertheless, the reported data are relatively

limited. Therefore, further studies are needed to effectively understand the role of nutrition on this outcome.

The findings of this review further demonstrate that there is little variation in the type of cognitive assessment, which in turn may partially contribute to the strength of some of the included studies. Notwithstanding, most of the included studies use the MMSE as one of the primary tools. One of the many advantages of this test is its ease of administration, despite the fact that it has been extensively criticized for its reliance on verbal interpretation. This can eventually prove to be a major problem when administering the test to illiterate participants.

An effective relationship between nutrition and polypharmacy is yet to be consolidated [133]. Since certain diseases *per se* increase the likelihood of poor nutritional status, it is difficult to determine the independent role of drugs on nutritional status. Comorbidity-adjusted correlations show a strong link between nutritional status and excessive polypharmacy (more than nine drugs), whereas polypharmacy (six to nine drugs) has no association with nutritional status in non-institutionalized older adults [133]. To the best of our knowledge, no study has been conducted to correlate nutritional status with polypharmacy in institutionalized elderly. Nevertheless, excessive polypharmacy was associated with declined nutritional status ($p=0.001$), functional ability ($p<0.001$) and cognitive capacity ($p<0.001$) when compared to the non-polypharmacy group [133]. These data may eventually suggest that adherence to healthy dietary patterns could potentially delay the onset of age-related health deterioration and reduce the need for multiple medications. The support of pharmacists and physicians in nursing homes would also be of great value in maintaining strict control of medications. Therefore, the prescription of multiple drugs will be monitored to ensure minimal risk to the health of older adults.

Several instruments have been used to assess malnutrition or its associated factors. Although most studies used MNA to assess the nutritional status of the elderly, slightly different cut-off points and criteria were used, which might ultimately lead to over- or underestimation. Some easy-to-implement changes, such as increasing tea consumption, may have substantial results in psychomotor and cognitive-related tasks. Considering that MNA does not measure the exact quantity or quality of fluid intake, further studies are needed to effectively understand the optimal type and quality of fluid intake in maintaining or improving the functional status of the elderly.

The strengths of this review, in our opinion, are the low prevalence of high RoB studies and the broader understanding of the potential benefits of an adequate nutritional status on

different outcomes, which, in our view, have not been adequately accounted for in the literature. However, most of the included studies were observational, thereby making it impossible to establish a cause-and-effect relationship. The fact that the clinicaltrials.gov database has not been included in the search strategy may eventually have contributed to the low rate of experimental studies included in the review, however the prevalence of clinical trials in domains outsides of medicines or similar are always very low, a some of the, if existing, could have been found in the searched databases. Besides, the subjective nature of domain assessment is prone to bias. By independently reviewing the domain ratings, we hope to better adjust the overall quality scores of the included studies. The highly heterogeneous nature of nutritional interventions on different outcomes increases the complexity of the analysis.

Our findings also include a few studies with low participation rates, which, when combined with variations in assessment methods, can eventually lead to inconsistencies that can hamper the reliability of the results.

In an aging society, with an increasing number of institutionalized elders, this review highlights the urgent need of further research on the relation of the nutritional status on functional capacity, cognitive status and polypharmacy in the elderly population living in nursing homes. Randomized clinical trials would be the most suitable approach to generate robust results.

2.5. Conclusion

The eight studies included in this systematic review show that better nutritional status is associated with better cognitive function and functional dependence in the elderly. An appropriate nutritional status and dietary nutritional management in institutionalized older adults is essential to preserve their health and quality of life.

Since nutritional status can be adjusted and has been reported to have very intricate links to cognition, independence and autonomy, a closer evaluation of nutritional status on these parameters is crucial to prevent associated health issues in the elderly population, especially the one that lives in nursing homes.

Chapter 3 | Daily Nutritional Intake and Nutritional Status: A Study in Institutionalized Older Adults in Viseu (Center of Portugal)

3.1. Introduction

Increased longevity is worldwide phenomenon that has made a significant impact on population distribution pyramids. Portugal is not an exception. Projections for 2050 suggest that the number of older adults will increase to 32% [134,135]. Central Portugal, which includes the district of Viseu, presents one of the highest aging indexes in the country. The aging population, new family structures and society dynamics and a growing insertion of women in the work market, can help explaining why many families choose to institutionalize their older adults [12,136]. Portugal has mixed long-term care, composed of a network of services, including care centers, home-based services and nursing homes ("residential structures for older people"). Nursing homes offer support through collective accommodation, meals, health care and leisure activities. Portugal has 3069 long-term care facilities (LTCFs) divided into 2445 general nursing homes, 287 residential homes, and 337 'mixed LTCFs' [96]. The institutionalization process is complex and involves many changes in daily life routines [135].

Malnutrition is a syndrome characterized by inadequate intake and absorption of nutrients [137] that is often underdiagnosed. In institutionalized older adults, malnutrition is becoming an alarming phenomenon and it has a large number of negative consequences, such as altered body cell mass and body composition leading to diminished physical and mental function and impaired clinical outcome from disease [138]. There is strong evidence that malnutrition has a negative impact in older adults' functional status and quality of life, increasing both morbidity and mortality [139].

A few studies suggest that malnutrition and/or the risk of malnutrition in older adults are influenced by nutritional care in nursing homes [140].

A balanced nutrition is an important and controllable factor in reaching and maintaining healthy old age. Older adults are a diverse population, vulnerable to nutritional inadequacies. Food intake is typically decreased in older adults and energy requirements are lower. Therefore, the challenge for older people is to meet the same nutrient needs but consuming fewer calories [64].

There is a lack of studies concerning dietary intake of the institutionalized older adults in Viseu. To the best of our knowledge no data exist concerning the relationship between dietary intake and nutritional status. Therefore, the present study was conducted, in a sample of institutionalized older adults in Viseu, in order to: a) estimate total energy and nutrients intake; b) evaluate the compliance with recommendations of energy, by macro and

micronutrients; and finally, to describe dietary intake according to nutritional status (assessed by MNA).

3.2. Material and methods

3.2.1. Subject recruitment and data collection

The present work is a cross-sectional study, performed with data collected from 15 Long-Term Care Institutions for the adults/nursing homes that accepted to collaborate in the study, and are located in the district of Viseu, Portugal. These nursing homes represent 90% of the total of the nursing homes in the city and they could be, either private or supported by the government. The inclusion criteria were subjects:(i) aged 65 or older, (ii) living in nursing homes at least for the last 3 months, (iii) presenting a BI upper or equal to 40 points and (iv) able to walk (with or without walking aid). The exclusion criteria were: (a) staying temporarily or living in the institution <3 months, (b) suffering from cognitive impairment, (c) presenting psychiatric disorders or dementia and (d) not accepting to take part in the survey. All participants gave written informed consent. Complete information on demographics, nutritional status, nutritional risk screening, functional and mental status, were routinely collected through self-report by trained researcher-administered standardized questionnaires. In demographics formal education was categorized according to years of formal education: 0 years= illiterate, 1-11 years, >11 years.

3.2.2. Nutritional Status of older adults

The socio-demographic data were collected via face-to-face questionnaire.

BMI was calculated as weight (kg)/height $(m)^2$, and classified according to Lipschitz [48]. Participants were weighed with a digital chair scale to the nearest 0.1kg.

Nutritional risk was settled by the MNA validated for Portuguese senior population (≥65 years) [141]. The MNA with a total score of 30 points consists of 18 questions, allowing several assessments: anthropometric assessment (BMI, weight loss, mid-arm circumference and calf circumference), global assessment (mobility, prescription drugs, independent life, psychological stress or acute disease, pressure sores or skin ulcers and neuropsychological problems), dietary assessment (full meals eaten daily, food intake decline, fluid consumption, protein intake, fruit and vegetable intake and mode of feeding) and self-assessment (self-view nutritional status and self-view health status). The MNA classifies individuals into three

categories as malnourished (<17 points), at risk of malnutrition (17–23.5 points) and normal nutritional status (≥24 points) [142].

3.2.3. Dietary intake of older adults

For the assessment of food intake, we used the three-day food record, and direct observation in three days (including weekend day). The three-day period always included one weekend day, taking into account possible differences in food consumption between weekdays and weekends. All food products, including beverages consumed were recorded per eating occasion and quantified and described as eaten. Dietary supplements, were not quantified. A nutritionist administered the survey measures, verified and quantified the food records. The amounts were recorded by the precise weighing method, weighing every portion served to individuals and the amount left on the plates at each meal [143]. Subsequently, the conversion of foods into nutrients was performed, using the Portuguese food composition table which was continuously adapted and updated and enabled [64]. For preparations which were not in the Portuguese food composition table recipes were disaggregated into raw ingredients allowing the description and quantification of each item. These obtained values for macronutrients and fiber were then converted into calories (using the Atwater factors) [144,145]. For analysis, the average of the three days was used.

3.2.4. Compliance with Energy and Nutrients Recommendations

The European Food Safety Authority (EFSA) Dietary Reference Values, were considered to determine the prevalence of adequate intake (AI) [71]. Reference intake ranges were used for macronutrients while for micronutrients, average requirements, AI or tolerable upper intake level were used. Based on recent clinical guidelines for older adults, for protein per kg of body weight, additional cut-offs (1 and 1.2g/kg) were used [73].

3.2.5. Ethics

The study protocol was performed in accordance with The Helsinki Declaration of Human Studies and approved by the Ethical Committee of the Polytechnic Institute of Viseu, Portugal (see appendix 1). All participants provided their written informed consent.

3.2.6. Statistical analysis

The collected data were analyzed using the IBM SPSS Statistics, version 28.0. The analysis of data involved descriptive statistics such as mean, standard deviation and frequencies. The

educational status, civil/marital status, BMI and MNA classes distributions by gender was analyzed by Qui-square tests. The energy and nutrients intake were previously analyzed by Kolmogorov-Smirnov tests to evaluate the continuity of the variables (parametric or non-parametric variables). The evaluation of energy and nutrients intake in comparison with DRI's was performed, according to gender, by Wilcoxon matched-pair signed-rank tests. The prevalence of inadequate intake of macronutrients was analyzed by gender with Qui-square tests. In the same way, the analysis of prevalence of inadequate intake of macronutrients, by gender, according to MNA classes was achieved by Qui-square tests. The average daily energy and nutrients intake, by gender, according MNA classes was evaluated by independent samples *t*-tests or Mann-Whitney tests, considering parametric or non-parametric variables. The level of significance of $p \leq 0.05$ was considered for all statistical analysis.

3.3. Results

3.3.1. *General Characteristics of the Population*

Table 3.1 summarizes the demographic and nutritional status (according BMI and MNA) of the participants. The mean age of the 214 homecare participants was 82.3±6.1 years, and 72% (n=154) were female. Most of them presented a low educational level (illiterate or 11 years of schooling =94.8%) and were widowed, separated or divorced (74.3%). Women were more likely than men to be widowed and less likely to get married. BMI values ranged from 16.0 kg/m^2 to 43.3 kg/m^2 with a median value of 28.3±4.9 kg/m^2. Based on Lipschitz classification [48], 7.5% of the subjects were underweight (BMI <22 kg/m^2), 34.6% were normal weight (BMI 22-27 kg/m^2), and 57.9% were overweight (BMI >27 kg/m^2). The percentages of men and women in the three BMI categories did not differ significantly. According to MNA, sixty participants were at risk of malnutrition (RM) (28.0%), and 154 (72.0%) well nourished (WN), with no significant differences between genders.

Table 3.1. Characteristics of nursing home residents by gender (n=214).

Variables	Total n (%)	Female n (%)	Male n (%)	*p-value*
Educational Status				
Illiterate	79 (36.9)	60 (75.9)	19 (24.1)	
1-11 years	124 (57.9)	87 (70.2)	37 (29.8)	0.549
>11 years	11 (5.1)	7 (63.6)	4 (36.4)	
Civil/Marital Status				
Single	25 (11.7)	20 (80.0)	5 (20.0)	
Married	30 (14.0)	14 (46.7)	16 (53.3)	0.004*
W/S/D	159 (74.3)	120 (75.5)	39 (24.5)	
BMI				
Underweight	16 (7.5)	10 (62.5)	6 (37.5)	
Normal	74 (34.6)	54 (73.0)	20 (27.0)	0.680
Overweight	124 (57.9)	90 (72.6)	34 (27.4)	
MNA				
At risk of malnutrition	60 (28.0)	48 (80.0)	12 (20.0)	0.102
Normal nutritional status	154 (72.0)	106 (68.8)	48 (31.2)	

W/S/D, widow, separated, divorced. BMI, body mass index; MNA, mini nutritional assessment. In brackets are the percentages: Qui-Square statistic tests was used to compare characteristics distributions by gender. *Statistical differences between gender were indicated by a p-value ≤0.05.

3.3.2. Energy and nutrients intake

Table 3.2. exhibits the mean dietary intakes of participants over a 3-day period by gender as measured by the precise weighing method and compares them with DRIs. The mean daily total energy intake (TEI) was 1729.1±317.3 Kcal/day (7.2±1.3MJ/day).

Gender comparisons revealed that women presented only vitamin B2 values according the recommendations whereas in men the compliance was observed for vitamin B2, C, E, potassium and iron. Regarding macronutrients, women and men presented high intakes of carbohydrates. An excessive fat intake was present in women while men presented lower intake. Thus, we might consider that in both men and women energy intake is made majoritarian by carbohydrates and by fat. Older adults (men and women) were below the EARs for fiber and for vitamin B12, D, E. They also presented calcium and magnesium intake

below the recommended levels, whereas excessive sodium intake was present. The studied population exceeded the tolerable upper intake for sodium (2000 mg/day) in 60%.

Table 3.2. Comparison between Dietary Reference Intake (DRI), energy and nutrients intake by gender in institutionalized older adults.

Variable		Female (n=154)			Male (n=60)		
		DRI Values	**Mean±SD**	***p-value***	**DRI Values**	**Mean±SD**	***p-value***
Energy (kcal/day)	60-69 years-old	1624	1708.0±309.2	0.002	2206.2	1783.5±333.7	<0.001
	≥70 years-old				1982.3		
Protein (g/day)		41	72.9±17.7	<0.001	54	78.0±19.7	<0.001
Fat (g/day)		54	55.6±19.1	<0.001	66	53.4±19.9	<0.001
Carbohydrates (g/day)		100	224,9±40.5	<0.001	100	231.5±38.6	<0.001
Dietary Fiber (g/day)		25	20.6±3.8	<0.001	25	21.6±4.9	<0.001
Water (ml/day)		2000	2313.7±373.4	<0.001	2500	2371.2±477.8	<0.001
Vitamin A (µg/day)		650	1089.7±255.3	<0.001	750	1080.4±259.6	<0.001
Vitamin B1 (mg/day)		0.8	1.2±0.3	<0.001	1.0	1.3±0.3	<0.001
Vitamin B2 (mg/day)		1.6	1.6±0.4	0.405	1.6	1.6±0.4	0.833
Vitamin B3 (mg/day)	60-69 years-old	12.5	16.8±4.7	<0.001	15.4	17.7±5.8	0.004
	≥70 years-old	12.3			15.2		
Vitamin B6 (mg/day)		1.6	1.9±0.5	<0.001	1.7	2.0±0.6	<0.001
Vitamin B12 (µg/day)		4	2.8±1.2	<0.001	4	2.9±1.5	<0.001
Vitamin C (mg/day)		95	105.0±35.3	<0.001	110	110.2±28.3	0.546
Vitamin D (µg/day)		15	3.9±3.0	<0.001	15	3.6±3.0	<0.001
Vitamin E (mg/day)		11	1.0±1.0	<0.001	13	0.9±0.9	0.133
Folic Acid (µg/day)		320	278.1±71.2	<0.001	320	280.8±73.6	<0.001
Sodium (mg/day)		2000	3347.7±753.2	<0.001	2000	3362.6±786.6	<0.001
Potassium (mg/day)		3500	3192.3±603.9	<0.001	3500	3332.5±703.0	0.065
Calcium (mg/day)		1000	776.7±227.1	<0.001	1000	818.3±224.0	<0.001
Phosphorus (mg/day)		550	1146.8±235.2	<0.001	550	1196.7±262.4	<0.001
Magnesium (mg/day)		300	248.1±47.3	<0.001	350	265.6±60.0	<0.001
Iron (mg/day)		11	9.3±1.9	<0.001	11	10.5±2.3	0.090
Zinc (mg/day)		9.3	8.7±2.2	0.002	11.7	9.6±2.9	<0.001
Selenium (µg/day)		70	4.3±4.4	<0.001	70	5.1±5.6	<0.001
Iodine (µg/day)		150	6.4±4.4	<0.001	150	6.0±4.2	<0.001

Wilcoxon matched-pair signed-rank tests was used to achieve pairwise differences between variables samples and their DRI values. Statistical differences between variables samples and their DRI values is indicated by a p-value ≤0.05.

Average contributions to the daily total energy intake (TEI) were 17.2±2.8% from protein, 28.1±6.7% from fat and 53.0±7.2% from carbohydrates, that were within the recommendations. On the other hand, fiber amount was 20.9±4.1g/day that was below recommendations (25g/day) (data not shown).

3.3.3. Compliance with recommendations of macronutrients

To calculate the prevalence of inadequacy of macronutrient intake, the guidelines proposed by EFSA for the European population and ESPEN were used [71,73]. The results were presented in table 3.3.

Table 3.3. Prevalence of inadequate intake of macronutrients by gender in institutionalized older adults.

	Total		**Female**		**Male**		***p-value***
	n	**%**	**n**	**%**	**n**	**%**	
Protein							
<1 g/kg weight	85	39.7	53	62.4	32	37.6	0.007
>1.2 g/kg weight	76	35.5	62	81.6	14	18.4	
Fat							
<20% TEI	23	10.7	13	56.5	10	43.5	0.009
>35% TEI	42	19.6	36	85.7	6	14.3	
Carbohydrates							
<45% TEI	36	16.8	25	69.4	11	30.6	0.307
>60% TEI	35	16.4	28	80.0	7	20.0	

%TEI - % of total energy intake. Qui-Square statistic tests was used to compare inadequate intake of macronutrients distributions by gender. Statistical differences between gender were indicated by a p-value≤0.05.

Only 24.8% of older adults presented a daily intake of protein according to recommendations by ESPEN guidelines, and 75.2% had inadequate intake of protein (39.7% below recommendations) [73]. 81.6% of elderly that presented intakes above 1.2 g/kg weight were women. The inadequacy of fat ingestion was observed in 30.3% of the studied population. Among them, the ingestion of excessive fat was observed in 19.6%. Women were more prone to consume excessive fat (85.7%) and carbohydrate (80.0%) than men (14.3% and 20.0%, respectively). The majority of older adults (66.8%) ingested carbohydrates according to recommendations. Statistically differences were found between gender in protein and fat, suggesting that women presented more inadequate intakes (mainly by excess).

3.3.4. *Dietary intake of energy and nutrients according to nutritional status evaluated by MNA*

None of the examined persons was defined as malnourished, as nobody obtained less than 17 points, in MNA evaluation. Table 3.4. shows the distribution of mean energy and nutrients intake of studied older adults by sex, according to their nutritional status. The balance of energy, macro and micronutrients intake between women at risk of malnutrition and with normal nutritional status, showed that older women at risk of malnutrition presented lower intakes of the majority of micronutrients, macronutrients and energy. Exceptions were found when we compared the daily intakes of carbohydrates, calcium iron and vitamin D. For these nutrients, no statistical differences were found between the two groups. The same tendency was found when comparing men at risk of malnutrition with those with normal nutritional status. In men, no differences were observed when the daily intake of carbohydrate, fat, vitamins B1, B12, C and calcium, sodium, potassium were compared between the two groups. When we consider the compliance with recommendations for energy, macronutrient and micronutrients of older women at risk of malnutrition and normal nutritional status we observed that both groups presented insufficient intakes of micronutrients, with exception of sodium, vitamin B1, vitamin C and phosphorus where the intakes are above the recommended intakes. For macronutrients the ingestion is above the DRI in both groups of older women. Women at risk of malnutrition had energy intakes slightly below the appropriate, while women with normal nutritional status presented higher energy intakes than recommended. Both group of men presented energy intake, fat intake, fiber and most of the micronutrient's intake below the appropriated levels. Only vitamin B1, phosphorus and sodium were above the recommendations.

Table 3.4. Average daily energy and nutrients intake according to nutritional status (Mean±SD).

		Female				Male			
		DRI values[1]	**At risk of malnutrition**	**Normal nutritional status**	***p-value***	**DRI values**[1]	**At risk of malnutrition**	**Normal nutritional status**	***p-value***
Energy (Kcal/day)[a]	60-69 years-old	1624	1621.2±326.0	1747.3±294.5	0.019*	2206.2	1635.7±326.8	1820.4±328.4	0.086
	≥70 years-old					1982.3			
Protein (g/day)[a]		41	66.5±19.6	75.9±16.0	0.002*	54	69.6±22.7	80.1±18.5	0.099
Carbohydrate (g/day) [a]		100	223.4±45.6	225.6±38.2	0.757	100	217.9±33.9	234.9±39.2	0.176
Fat (g/day) [b]		54	49.5±19.2	58.3±18.4	0.003*	66	47.9±16.4	54.8±20.6	0.327
Water (g/day) [a]		2000	2204.4±382.7	2363.3±360.1	0.014*	2500	2015.9±497.8	2460.0±434.0	0.003*
Fiber (g/day) [a]		25	19.3±3.8	21.2±3.6	0.004*	25	17.7±5.1	22.6±4.3	0.003*
Vitamin B1 (mg/day) [b]		0.8	1.2±0.3	1.3±0.3	0.013*	1.0	1.2±0.2	1.3±0.3	0.330
Vitamin B12 (µg/day) [b]		4	2.5±1.3	2.9±1.2	0.032*	4	2.3±1.4	3.0±1.5	0.125
Vitamin C (mg/day) [b]		95	95.5±35.1	109.2±34.8	0.013*	110	97.2±35.1	113.5±25.7	0.157
Vitamin D (µg/day) [b]		15	3.6±2.7	4.1±3.2	0.428	15	3.6±2.4	3.6±3.2	0.725
Folic Acid (µg/day) [b]		320	256.9±70.7	287.8±69.6	0.008*	320	239.7±83.6	291.0±68.1	0.028*
Calcium (mg/day) [b]		1000	762.7±224.9	783.0±228.8	0.608	1000	818.3±305.9	818.3±202.7	1.000
Iron (mg/day) [b]		11	9.0±2.1	9.5±1.8	0.223	11	9.2±3.0	10.8±2.0	0.038*
Zinc (mg/day) [b]		9.3	7.9±2.3	9.1±2.1	0.003*	11.7	8.0±2.8	10.0±2.8	0.059
Magnesium (mg/day) [a]		300	234.2±48.2	254.3±45.7	0.014*	350	232.5±63.5	273.8±56.8	0.032*
Sodium (mg/day) [a]		2000	3124.0±755.0	3449.0±733.7	0.013*	2000	3174.3±859.10	3409.6±769.9	0.358
Potassium (mg/day) [a]		3500	3011.8±626.5	3274.0±578.0	0.012*	3500	3098.9±794.4	3390.8±674.8	0.201
Phosphorus (mg/day) [a]		550	1081.4±253.6	1176.5±221.4	0.020*	550	1098.2±313.9	1221.3±245.6	0.148

[1] EFSA Dietary Reference Values for nutrients (2017). Statistical differences between classes of nutritional status were achieved with (a) Independent samples *t*-tests or (b) Mann-Whitney tests, by average daily energy and nutrients intake. *Statistical differences between classes of nutritional status were indicated by a p-value ≤0.05.

3.4. Discussion

The current study evaluated the nutritional status and dietary intakes, as well as their adequacy, in a sample of older adults institutionalized in Viseu, a region located in center Portugal. Furthermore, this study examined the association between energy/nutrients intake and nutritional status.

This group of institutionalized Portuguese older adults presented an average of age of 82.3±6.1 years old was mainly female, with low level of instruction and currently without a partner. These characteristics were observed in other Portuguese studies with institutionalized participants [146,147]. Life expectancy, known to be higher in women, and the excess of male mortality, help explain this phenomenon [148].

In old age, good nutritional status is critical for maintenance of health and quality of life. Nutritional screening, assessment and interventions in this age are essential to treat and prevent malnutrition [140,149]. There are several valid and reliable screening tools that can and should be used [142].

The evaluation of nutritional status using MNA indicated that malnutrition was absent in this studied population. However, the prevalence of risk of malnutrition was 28.0%, with no significant differences between gender. Although the percentage of older adults at risk of malnutrition was below than found in other studies, it is important to screen these elderly [140,150].

The current study used the dietary reference values published by EFSA in 2017 [71]. Adequate energy and nutrients intake are known to be important to the nutritional status of elderly [151]. Daily energy of studied older adults was 1729.1±317.3 Kcal. This value was similar to the daily energy obtained in *National Food, Nutrition and Physical Activity Survey of the Portuguese General Population* [152]. In summary, this study has shown that overall intakes of macronutrients are generally sufficient. However, this particular population group have high intakes of carbohydrates and sodium, and low intakes of dietary fiber, vitamin D and calcium, compared to recommendations. Dietary fiber value is usually low in elderly, so it's important to adjust intakes to prevent gastrointestinal problems, like constipation and diarrhea, that are commonly among older adults [73]. According to have been observed in the general European population and in Portuguese population, in particular, there is a high prevalence of sodium inadequacy, more pronounced in men, which is associated with cardiovascular events and mortality [144,153,154]. It is known that there is an increase in the consumption of sugar and salt by the elderly due to changes in taste perception. Sufficient calcium intake is necessary not only for preserve bone health, but it also has a role in other diseases, such as colorectal cancer

[155,156]. The studied population presented low ingestion of vitamin B12, in accordance of the presented by other Portuguese studies [152,157]. Additionally, inadequate calcium and vitamin D intake was confirmed in the present study in line with what was reported by others [157,158]. These deficits are associated with higher risks of falls and fractures, as well as osteoporosis and osteopenia, conditions that have high impact on the quality of life of older adults [159,160]. The low consumption of calcium, associated with a low efficiency of its absorption, condition precipitated by achlorhydria and low circulating levels of 1.25 dihydroxy D vitamin, contributes to the reduction of the reserves of this mineral, leading to bone diseases in older adults.

In the present study, the intake of micronutrients was estimated of current or usual intake. It is well known that blood measures of nutrients may provide a more accurate and objective measure of diet. However, the measurement of some nutrients is expensive and quite complex, moreover obtained results might not reflect the real intake of the nutrient due to seasonal variations or metabolism [161,162].

Our study shown an average contribution of macronutrients to daily total energy intake (TEI) of 17.2±2.8% from protein, 28.1±6.7% from fat and 53.0±7.2% from carbohydrates. These values were within the reference intake range, recommended by EFSA, and considered for a balanced diet [144]. However, more than 80% of older women had intakes above the recommended upper threshold of 35% for fat and 60% for carbohydrates. These values are in accordance to other studies in Portugal [152] and Ireland [163]. Yet, this study considered the total carbohydrate, so the mean intake of free sugars in older adults is lacking, as well as the mean of saturated fatty acids.

According to recent guidelines additional cut-offs for protein were established for older adults [73]. This dietary recommendations for protein are aimed at preventing deficiencies and are based on nitrogen balance [73]. In this study, more than one-third (39.7%) of older adults had low protein intake. Men were more prone to consume low protein (37.6%) while women ingested more protein (81.6%). The insufficient protein intake can lead to age associated loss of skeletal muscle mass and strength (sarcopenia) and to functional decline [164]. Our results of inadequate protein intake are in line with previous studies [165,166].

Older men and women, at risk of malnutrition, presented lower intakes of the majority of micronutrients, macronutrients and energy. These results were similarly to the survey conducted among Turkish NH residents (n=554), where energy and nutrients intake stayed higher in older people who had a normal nutritional status compared to those at risk of malnutrition [140]. Low intakes of energy and micronutrients among residents at risk of

malnutrition are known to be common [67,140]. When we consider the compliance with energy, macronutrient and micronutrients recommendations of older women at risk of malnutrition and normal nutritional status, we observed that both groups presented insufficient intakes of micronutrients, with exception of sodium, vitamin B1 and phosphorus, where the intakes are above the recommended intakes. For macronutrients, the ingestion is above the DRI in both groups of older women. Women at risk of malnutrition had energy intakes slightly below the appropriate, while women with normal nutritional status presented higher energy intakes than recommended. Both group of men presented energy intake, fat intake, fiber and most of the micronutrient's intake below the appropriated levels. Only vitamin B1, phosphorus and sodium were above the recommendations. One hypothesis is that MNA does not distinguish subjects according to nutrients adequacy. In the present study, the intake of nutrients was not only inadequate in residents who were at risk of malnutrition, but also in those with normal nutritional status. Other authors have observed a poor energy and vitamin intake in a large proportion of older adults classified as having normal nutritional status [118].

3.5. Limitations of the study

Dietary Reference Value is expressed as grams per body weight, and here actual weight was used. Some studies recommend using adjusted body weight, because in overweight persons the weight in excess is mainly fat mass, resulting in an overestimation of protein requirements [165]. However, may also be problematic and introduce some error, the choice and definition of the 'healthy' weight to adjust the protein needs. Moreover, the present study only considered total carbohydrates and total fat. A perception of added sugar and of the lipidic composition of diet will allow to more reliable conclusions.

3.6. Conclusions

In conclusion, this study has shown that this population group had high intakes of total fat, carbohydrate and salt and low intakes of dietary fiber and micronutrients, such as vitamin B12, D and E, calcium and magnesium. Women were more prone to present deficiency than men. Moreover, this population presented inadequate ingestion of protein (75.2%), fat (30.3%) and carbohydrate (33.2%).

None of the examined people were defined as malnourished assessed by MNA. The comparison of energy, macro and micronutrients intake between institutionalized older adults

at risk of malnutrition and with normal nutritional status showed that older women and men at risk of malnutrition presented lower intakes of the majority of micronutrients, macronutrients and energy. Moreover, older women at risk of malnutrition and normal nutritional status presented insufficient intakes of micronutrients, while for macronutrients the ingestion were above the DRI for both. In both group of men, the intake of energy, fat, fiber and most of the micronutrients, were below the appropriated levels.

The present findings also support the importance of regular evaluation of the nutritional status and encourage healthy eating, as an essential contribution to a successful aging.

Chapter 4 | The Relationship between Nutritional Status and Functional Capacity: A Contribution Study in Institutionalized Portuguese Older Adults

Adapted from:

Caçador, C., Teixeira-Lemos, E., Oliveira, J., Pinheiro, J., Mascarenhas-Melo, F., & Ramos, F. (2021). The Relationship between Nutritional Status and Functional Capacity: A Contribution Study in Institutionalized Portuguese Older Adults. *International journal of environmental research and public health*, 18(7), 3789. https://doi.org/10.3390/ijerph18073789

4.1. Introduction

Aging is a global phenomenon that has a significant impact on population pyramids [134]. Increase in life expectancy, declining fertility, mortality rates, and reduced population growth are key factors that result in increasing numbers, thus leading to an increase in the proportion of adults over 65 years of age [167]. In Europe, the older adults accounted for 15% of the total population in 1971, 20% in 2000, and it is expected to reach 35% in 2050 [148]. In Portugal, the scenario is similar. The prevalence of the older person ranged from 8% in 1960 to 17% in 2007, and projections for 2050 suggest that the number will increase to 32% [134,135]. It is worth noting that population distribution is not homogeneous across countries. For instance, Central Portugal, which includes the district of Viseu, presents one of the highest aging indexes in the country.

The demographic aging of the population allied with the new family structures and societal dynamics is generating an increasing demand for institutions for the older adults [168]. The lack of family support or decent housing, insufficient economic resources, and the increasing insertion of women in the labor market are some of the factors that justify why families resort to institutionalization [136]. The institutionalization process is complex and involves radical changes in daily life routines [96]. As a consequence, a deterioration of the nutritional, cognitive and functional status is observed.

Malnutrition is becoming an alarming phenomenon among institutionalized older adults and is oftentimes underdiagnosed. In the general population, this condition has a prevalence rate between 5% - 12%, while in institutionalized adults, the prevalence is as high as 52% - 85%, depending on the criteria and methodology used in each study [33]. In the older person, malnutrition increases morbidity and mortality, reduces quality of life, and increases the length of hospital stay. Furthermore, malnutrition is associated with deteriorating functional status, weakening of the immune system, increased risk of infections, poor wound healing, and sarcopenia [167].

Continuous assessment of the nutritional status, functioning and cognitive ability of institutionalized older adults is crucial not only to prevent their dramatic decline, but also to improve the quality of life in this population [169]. Although functional and cognitive abilities and malnutrition are reported to be very closely linked to each other, the differential association between nutritional risk and nutritional status with incidence in disability for basic activities of daily living and cognitive impairment remains limited. The present study aims to: (i) characterize the nutritional and functional status of an institutionalized population in one

of the most rapidly aging regions of Portugal, (ii) examine the possible relationship between nutritional status (as evaluated by the BMI and WC) and nutritional risk (as measured by MNA), and (iii) study whether nutritional status and nutritional risk could be associated with a decrease in functional outcomes for activities of daily living (as assessed by BI) and with cognitive impairment (as assessed by MMSE) in institutionalized older adults.

4.2. Materials and Methods

4.2.1. Subject recruitment and data collection

A cross-sectional study was conducted using data collected from residents living in home-care residences throughout the district of Viseu (Portugal). The inclusion criteria were subjects: (i) aged 65 or older, (ii) living in nursing homes for at least the last 3 months, (iii) presenting a BI ≥40 points, (iv) able to walk (with or without walking aid) and (v) who accepted to participate in the study. The exclusion criteria were: (a) staying temporarily or living in the institution for <3 months, (b) suffering from cognitive impairment, (c) presenting psychiatric disorders or dementia, and (d) refusing to participate in the survey. Data were collected in 15 institutions. All participants gave their written informed consent for inclusion before they participated in the study. The study was conducted in accordance with the guidelines of the World Medical Association's Declaration of Helsinki (as revised in Brazil 2013), and the protocol was approved by the Ethics Committee of the Polytechnic Institute of Viseu (see appendix 1) (Ref. 01/sub/2021). Complete information on demographics, nutritional status, nutritional risk screening, functional and mental status, was routinely collected through self-report using standardized questionnaires administered by trained researchers. In demography, formal education was categorized according to the years of formal education: 0 years = illiterate, 1-11 years, >11 years.

4.2.2. Anthropometric measurements and nutritional indicators

WC and BMI were used to assess nutritional status according to standard criteria. Anthropometric measurements, such as weight, height and WC, were undertaken. Height (rounded to the nearest 0.1 cm) was measured using a measuring tape, with participants standing upright against a wall without shoes. WC was defined as the midpoint between the lower rib and the upper margin of the iliac crest and was measured to the nearest 0.1 cm. WC classifications were based on the cut-off values recommended by the National Cholesterol

Education Program Adult Treatment Panel III (NCEP ATP III): high risk of cardiovascular disease when WC ≥102 cm in males and ≥88 cm in females. When the older person had deformations of the spinal column, the sitting knee height was measured in accordance with Chumlea and co-workers [170]. BMI was calculated as weight (kg)/height $(m)^2$ and classified according to Lipschitz [48]. Participants were weighed using a digital chair scale to the nearest 0.1 kg.

Nutritional risk was established by the MNA, which was validated for the Portuguese older adult population (≥65 years old) [141]. The MNA with a total score of 30 points consists of 18 questions, allowing several assessments: anthropometric assessment (BMI, weight loss, mid-upper arm circumference and calf circumference), global assessment (mobility, prescription drugs, independent life, psychological stress or acute disorder, pressure sores or decubitus ulcers and neuropsychological problems), dietary assessment (complete meals eaten daily, decline in food intake, fluid consumption, protein intake, fruit and vegetable intake and mode of feeding) and self-assessment (self-view of nutritional status and self-view of health status). The MNA classifies individuals into three categories: as malnourished (<17 points), at risk of malnutrition (17–23.5 points), and normal nutritional status (≥24 points) [142].

4.2.3. Performance in Activities of Daily Living (ADL)

BI is an index used to evaluate the functional ability of the older adult in 10 ADL (ambulation, chair/bed transfers, bathing self, personal hygiene, stair climbing, feeding, toileting, bowel control, bladder control, dressing). The total score of BI ranges from 0 to 100 points and classifies the individuals' level of dependence as follows: <20, totally dependent; 20–39, very dependent; 40-59, partially dependent; 60–79, minimally dependent; and 80–100, independent [171].

4.2.4. Cognitive Performance

Cognitive status was evaluated by the MMSE validated for the Portuguese population [172]. This is one of the most widely used instruments as a screening for cognitive impairment. It includes 30 items, which assesses temporal and spatial orientation, working memory, recall, attention, arithmetic capacity, linguistic, and visual-motor skills. The maximum score is 30 points (one point per correct item). The minimum cut-off value for adequate cognitive functioning is set accordingly to the level of education of the participant. In this study,

cognitive impairment was defined using the following score cut-off points: ≤15 for illiterate, ≤22 for subjects with 1-11 years of education, and ≤27 for people > 11 years of education [173].

4.2.5. Statistical analysis

The collected data was analyzed using IBM SPSS Statistics, version 26.0. Data analysis included descriptive statistics such as mean, standard deviation and frequencies. The independent variables t-test or the analysis of variance (ANOVA) with Bonferroni post-hoc tests were used to compare the means of the continuous variables according to the MNA and BMI classes. The effects of gender and age (by classes) were performed using Chi-Square tests, considering counting variables. Pearson's Correlation was used to evaluate correlations between continuous variables. The significance level of $p<0.05$ was considered for all statistical analyses.

4.3. Results

4.3.1. General Characteristics of the Population

Table 4.1 summarizes the demographic, nutritional, functional and mental status of the study participants. The mean age of the 214 homecare participants was 82.3±6.1 years, and 72% (n=154) were female. Most of them presented a low educational level (illiterate or 11 years of schooling =94.8%) and were widowed, separated or divorced (74.3%). Women were more likely than men to be widowed and less likely to get married. On average, men had a higher WC than women (101.9±10.0 vs 94.6±10.5), but there were no significant differences between men and women in the percentages of participants with WC above the risk cut-offs (102 cm for men and 88 cm for women) [174]. BMI values ranged from 16.0 kg/m^2 to 43.3 kg/m^2 with a median value of 28.3±4.9 kg/m^2. Based on Lipschitz classification [2], 7.5% of the subjects were underweight (BMI <22 kg/m^2), 34.6% were normal weight (BMI 22 – 27 kg/m^2), and 57.9% were overweight (BMI >27 kg/m^2). The percentages of men and women in the three BMI categories did not differ significantly. Sixty participants were at risk of malnutrition (RM) (28.0%), and 154 (72%) were well nourished (WN) with no significant gender differences. BI scores indicated that the majority of patients (69.6%) were minimally dependent on ADL. A total of 84 (39.3%) participants presented cognitive impairment

through the MMSE screening (Table 4.1). Among them, women were more affected than men (p<0.01).

Table 4.1. Population demographics, nutritional, functional and cognitive characteristics by gender.

Variables	Total	Female	Male	*p*-value
Educational Status				
Illiterate	79 (36.9)	60 (39.0)	19 (31.7)	
1-11 years	124 (57.9)	87 (56.5)	37 (61.7)	0.549
>11 years	11 (5.1)	7 (4.5)	4 (6.7)	
Civil Status				
Single	25 (11.7)	20 (13.0)	5 (8.8)	
Married	30 (14.0)	14 (9.1)	16 (26.7)	0.004
W/S/D	159 (74.3)	120 (77.9)	39 (65.0)	
WC				
Normal	132 (61.7)	100 (64.9)	32 (53.3)	0.080
High risk	82 (38.3)	54 (35.1)	28 (46.7)	
BMI				
Underweight	16 (7.5)	10 (6.6)	6 (10.0)	
Normal	74 (34.6)	54 (35.1)	20 (33.3)	0.680
Overweight	124 (57.9)	90 (58.4)	34 (56.7)	
MNA				
At risk of malnutrition	60 (28.0)	48 (31.2)	12 (20.0)	0.102
Normal nutritional status	154 (72.0)	106 (68.8)	48 (80.0)	
BI				
Partially dependent	14 (6.5)	11 (7.1)	3 (5.0)	
Minimally dependent	149 (69.6)	108 (70.1)	41 (68.3)	0.739
Independent	51 (23.8)	35 (22.7)	16 (26.7)	
MMSE				
Cognitive impairment	84 (39.3)	69 (44.8)	15 (25.0)	0.008
Without cognitive impairment	130 (60.7)	85 (55.2)	45 (75.0)	

Note: W/S/D, Widow/Separated/Divorced; WC, Waist Circumference; BMI, Body Mass Index; MNA, Mini Nutritional Assessment; BI, Barthel Index; MMSE, Mini Mental State Examination. In brackets are the percentages: Statistical comparisons between genders.

4.3.2. Age effect on nutritional status, nutritional risk, self-dependence in activities of daily living and cognitive performance

In Table 4.2, MNA, BMI, WC, BI and MMSE are reported according to age classes. There were no differences according to age in any of the different variables.

Table 4.2. Age effects on nutritional status, nutritional risk, self-dependence in activities of daily living and cognitive status.

		Age groups			*p-value*
		65-76	77-86	87-99	
MNA					
	At risk of malnutrition	10 (16.7)	33 (55.0)	17 (28.3)	0.599
	Normal nutritional status	35 (22.7)	81 (52.6)	38 (24.7)	
BMI					
	Underweight	1 (6.3)	8 (50.0)	7 (43.8)	
	Normal	20 (27.0)	37 (50.0)	17 (23.0)	0.225
	Overweight	24 (19.4)	69 (55.6)	31 (25.0)	
WC					
	Normal	29 (22.0)	64 (48.5)	39 (29.5)	0.165
	High risk	16 (19.5)	50 (61.0)	16 (19.5)	
BI					
	Partially dependent	3 (21.4)	8 (57.1)	3 (21.4)	
	Minimally dependent	10 (24.4)	22 (53.7)	9 (22.0)	0.943
	Independent	32 (20.1)	84 (52.8)	43 (27.0)	
MMSE					
	Cognitive impairment	20 (23.8)	43 (51.2)	21 (25.0)	0.723
	Without cognitive impairment	25 (19.2)	71 (54.6)	34 (26.2)	

Note: MNA, Mini Nutritional Assessment; BMI, Body Mass Index; WC, Waist Circumference; BI, Barthel Index; MMSE, Mini Mental State Examination

4.3.3. Effect of nutritional status and nutritional risk in functional and cognitive performance

The influence of nutritional status on nutritional risk, functional and cognitive performance was evaluated. The results showed that MNA was statistically different between the classes of BMI ($p<0.001$) and BI ($p<0.05$); nevertheless, there were no differences when considering cognitive evaluation (Table 4.3).

Table 4.3. Participants' nutritional risk and functioning based on their BMI categorization.

Variables	**BMI**			***p-value***
	Underweight	Normal	Overweight	
MNA	21.8±2.5 [a]	25.0±2.0 [b]	25.3±2.2 [b]	< 0.001
BI	74.7±18.5 [a]	84.8±15.7 [b]	86.0±14.4 [b]	0.021
MMSE	19.0±5.6	21.1±4.9	21.1±5.3	0.295

Note: MNA, Mini Nutritional Assessment score; BI, Barthel Index; MMSE, Mini Mental State Examination. [a,b] Values within rows with different superscripts are significantly different.

4.3.4. Nutritional risk

Malnutrition was not observed among the residents; however, 28% of the study population was found to be at risk of malnutrition (Table 4.1). The influence of MNA on the ability to perform ADL and on cognitive status was verified (Table 4.4).

Table 4.4. Participants' nutritional status and functioning based on their MNA categorization.

Variables	MNA		*p-value*
	At risk	Well nourished	
BMI (kg/m^2)	27.1±5.6	28.8±4.5	0.018
BI	77.0±17.8	87.7±13.2	< 0.001
MMSE	19.3±5.6	21.6±4.9	0.003

MNA: mini nutritional assessment; BMI: body mass index; BI: Barthel index; MMSE: mini mental state examination; WC: waist circumference.

These observed differences between the MNA scores were significant (p<0.05). The results indicated that the improvement in nutritional status was accompanied by an increase in BMI and an improvement in BI and cognitive function. Thus, it is evident that the risk of malnutrition increases the dependence of residents.

The correlation analysis between nutritional status, nutritional risk, and functional and mental disability assessment (BI and MMSE) is shown in Table 4.5. There were no correlations between nutritional status (BMI and WC) and BI and MMSE. However, a slightly positive correlation was observed between nutritional status and nutritional risk (p<0.001). MNA had a moderate positive correlation with BI and MMSE. Therefore, the ability to perform ADL and cognitive functions is directly related to a comprehensive nutritional assessment measured by the MNA in institutionalized older adults.

Table 4.5. Correlation between nutritional status, nutritional risk, and functional and mental disability.

Variables	BMI		WC		MMSE		BI	
MNA	0.28	(<0.001)	0.13	(0.059)	0.30	(<0.001)	0.40	(<0.001)
BMI			0.72	(0.715)	0.08	(0.239)	0.09	(0.169)
WC					0.01	(0.899)	-0.04	(0.572)
MMSE							0.35	(< 0.001)

MNA: mini nutritional assessment; BMI: body mass index; BI: Barthel index; MMSE: mini mental state examination; WC: waist circumference.

4.4. Discussion

The present study characterized a population of institutionalized Portuguese older adults and evaluated the association between their functional performance, cognitive ability, nutritional status and nutritional risk.

The study population was mainly female with less than four years of schooling and mostly without a partner (single, widowed, separated or divorced). These characteristics were observed in other Portuguese studies with institutionalized individuals [146,147]. This phenomenon may be related to excess male mortality and life expectancy, which is known to be higher in females [148]. Longer life expectancy often translates into more health problems that, besides physiological differences in brain structure and function, may explain sexual variation in cognitive aging [175,176]. In fact, deficits in cognition were observed to be significantly different between males and females with higher prevalence among women. Few studies mentioned significant differences in gender-based cognition, while others reported no difference [177,178]. In addition, this study showed a moderate vulnerable older adult population, with minimal dependence on ADL (69.6%) and impaired cognition (39.3%).

Age is a well-documented factor that contributes to the progressive decline in cognitive and functional abilities and makes individuals prone to nutritional deficiencies [167]. However, in this study, age was not considered a predictive factor for nutritional status or risk, self-dependence in ADL, and cognitive status. In fact, different authors have suggested that there are other risk factors more powerful than considering age. Comorbidities such as diabetes, hypertension, and obesity and educational level are some examples [179]. Hence, since our sample constitutes 88.8% of low educational level (illiterate or fourth year of schooling or less) and have considered age with other comorbidities, there may be an additional effect of confusion associated with age.

Overweight or obese patients are often identified by BMI, which is an objective measure of body fat based on height and weight. High BMI is considered a risk factor for the health of the older person, since it is associated with deterioration in quality of life and high rates of morbidity and mortality [180]. BMI characterized 57.9% of individuals to be overweight. Although being overweight is associated with a decrease in physical well-being, the individuals studied did not show an impaired ability to perform normal activities of daily living, as the BI values were similar to those with normal BMI [181]. The use of BMI as a surrogate for adiposity is controversial in older adults: (i) individuals lose height on aging creating an overestimation of BMI values [182]; (ii) BMI fail on identifying older adults with obesity and it

is unable to distinguish between peripheral and visceral obesity. Therefore, older adults with central obesity presenting a normal BMI may also be at risk for adverse cardiometabolic dysfunction [183,184]. Moreover, the continuously loss of muscle mass during the aging process when it is associated with obesity (sarcopenic obesity) can go unnoticed suggesting that it is possible to have a high BMI and be inappropriately nourished [185]. These considerations lead to a reflection about the measures for weight management in institutionalized older adults. In the present study the high incidence of independent overweight individuals suggests a medical/nutritional evaluation in order to manage the benefits vs. the risks of any future interventions. Low weight seniors (7.5%) presented a significant decrease in physical abilities, while no differences in mental well-being were verified. These results might be assigned to a decrease of activity due to malnutrition or sarcopenia.

Anthropometric values (e.g. BMI and WC) were closely related to nutritional status, providing detailed information on the different components of the body structure, especially the muscular and fatty components [181]. A positive correlation was observed between BMI and WC and nutritional risk; however, statistical significance was only achieved between BMI and MNA score, despite this correlation not being strong. As expected, a strong correlation ($r=0.72$) was verified between both anthropometric values. Although only 34.6% of the institutionalized older adults had normal BMI, the MNA assessment indicated that 72% of the population had a normal nutritional status. This discrepancy is explained by the multifactorial variables evaluated in MNA, besides anthropometric values, which provide a closer insight to whether the older adults are adequately nourished or not [142].

In comparison with other studies conducted in Europe, similar frequencies for risk of malnutrition were observed: 42% in Germany, 51% in Spain, 46% in Italy as compared to 42.7% in our study [185–187]. Thus, much work remains to be done in the institutionalized older adults to balance their nutritional status.

In line with the previous observations, the older adult studied at risk of malnutrition presented significantly increased cognitive impairment compared to the well-nourished.

A slightly positive correlation was found between MNA scores and MMSE values ($r=0.3$, $p<0.0001$). Previous studies conducted in other institutions also demonstrated a correlation between nutritional status and cognitive function. Malnourished older adults or even at risk of malnutrition presented lower cognitive abilities than those with a normal nutritional status [117].

Similarly, different studies obtained an equivalent relationship between malnutrition and functional dependence [188]. Lower BI scores were found mainly in the poorly nourished older adult than in those with better nutritional status. Our research showed a positive correlation between MNA and BI ($r=0.4$, $p<0.0001$). In general, well-nourished individuals perform better in ADL.

Cognitive and functional abilities were also found to be interconnected ($r=0.35$, $p<0.0001$). Previously, a systematic review pointed to a strong but unilateral association between cognitive and functional impairment [96]. Deficits caused by cognitive decline can lead to disability, thereby reducing and/or losing the ability to perform activities of daily living. However, functional impairment does not result in deterioration of cognitive functions.

Although statistical significance was observed between the variables, the correlation values were weak. However, these results do not invalidate the relationship between nutritional, cognitive and functional status. On the contrary, these findings reinforce the need to monitor and intervene in each of these areas to enhance a balanced quality of life.

Studying this sample of older adults does not allow to generalize the obtained results to the whole institutionalized Portuguese seniors. However, to the best of our knowledge, this study is the first to differentially evaluate nutritional, cognitive and functional status in institutionalized Portuguese older adults. Nevertheless, the absence of randomly sampling and, also, the sample size, limits the representativity of the study. A larger random sample would possibly have strengthened correlation values between nutritional, cognitive and functional abilities. Besides, the results may be biased due to the refusal to participate in the study and the nature of the responses given in the questionnaire. Cognitive impairment may influence MNA responses, since memory problems make it difficult for people to remember factors related to the type of ingested food or liquids and even the number of meals per day. In addition, the exclusion criteria could also withdraw the strength of the correlations, as individuals with strong cognitive and functional impairments were not included in the study. However, there is no reason to believe that considering these weak points will drastically change the results.

4.5. Conclusions

This cross-sectional study shows a moderately vulnerable older adult population. Most of the older adults presented minimal functional dependence on ADL, normal nutritional status, and no cognitive impairment. A differential interdependence was found between nutritional, cognitive and functional status. The risk of malnutrition is related to higher functional dependence and cognitive impairment. The need to implement cognitive and motor stimulation programs, as well as interventions aimed at enhancing a correct diet, has been reinforced in order to preserve the nutritional, cognitive and functional capabilities in institutionalized older adults. These programs should focus on achieving greater levels of independence and autonomy, thereby leading to an improvement in self-care and overall well-being of these populations.

Chapter 5 | The Prevalence of Polypharmacy and Potentially Inappropriate Medications and Its Relationship with Cognitive Status in Portuguese Institutionalized Older Adults: A Cross-Sectional Study

Adapted from:

Caçador C., Teixeira-Lemos E., Oliveira J., Pinheiro J., Teixeira-Lemos L., Ramos F. The Prevalence of Polypharmacy and Potentially Inappropriate Medications and Its Relationship with Cognitive Status in Portuguese Institutionalized Older Adults: A Cross-Sectional Study. *International Journal of Environmental Research and Public Health*. 2022; 19(5):2637. https://doi.org/10.3390/ijerph19052637

5.1. Introduction

The aging process allied with the increase in life expectancy leads to higher prevalence of multimorbidity worldwide [189]. Portugal, with the third higher aging index in Europe in 2018, is no exception [168]. Currently, 81.5% of people over 85 years old experience multimorbidity (defined by two or more chronic diseases) [109], which by consequence, increases drug consumption and the risk of polypharmacy [110]. Polypharmacy is defined as the use of multiple medications by a patient; there is no standardized minimum threshold for the number of medicines one takes in a day [97]. Age is a risk factor for polypharmacy with 20 to 30% of older adults taking more than four medications. The process of institutionalization worsens the situation and, on average, nursing home residents take more than eight drugs per day [98].

Polypharmacy, besides increasing health care costs, is also associated with other negative consequences [99]. Individuals who take multiple medications are at higher risk of adverse drug events, drug interaction and potentially inappropriate medication (PIM) [99]. Older people are even more susceptible to these effects due to age-related physiological changes that can alter drug pharmacokinetics and pharmacodynamics, impacting hepatic elimination and renal excretion [100]. It is estimated that 51% of the reported adverse drug events were presumably preventable [101]. Furthermore, in this age group, polypharmacy is also often associated with physical dysfunction and cognitive decline [102].

In elderly, a fine line separates polypharmacy and the risk of PIM. On one hand, to meet several clinical guidelines, polypharmacy is required [98]. For instance, three medications are often required to manage symptoms of heart failure or control blood pressure and, at least, two medications for efficient glucose control [103]. On the other hand, as PIM is defined as drugs with ineffectiveness or high risk–benefit ratio, evidence shows that the reduction of ingested drugs decreases the risk of PIM without compromising health status [103,104].

To minimize the occurrence of PIM, and subsequently inappropriate polypharmacy, it is essential to consider the risk-benefit ratio of each drug. The Beers Criteria is one of the most used methods to assess PIM use [100]. These guidelines are frequently revised by the American Geriatric Society, listing the medicines that should be typically avoided by older adults in ordinary conditions or under specific situations, such as in certain diseases or conditions [105]. The updated version of the Beers Criteria includes a separate PIM list for people with dementia and delirium, recognizing the importance of management of these medications in this older adult subset. It has also been reported that patients with dementia are prescribed an average of 5 to 10 drugs, with most treatments indicated for other

comorbid medical conditions [190]. For instance, the use of multiple medications in this population, particularly anticholinergic and sedative agents, may worsen memory loss and increase functional impairment [191].

Yet, even with the application of diverse tools, studies demonstrated that PIM is still a concern among older people. Of note, institutionalized seniors are the most frequently exposed to PIM [192,193]. Estimations indicate that this practice ranges from 18% to 48.7% in outpatients, 13-15% to 54% in hospitalizations and 37% to 67% in nursing home residents [194]. The implementation of simple and effective action projects for drug therapy management are essential to avoid and control PIM prescription and, thereby, contribute to the improvement of elderly life quality [195,196]. The study performed by Simões *et al.* (2019) concerning the prevalence of potentially inappropriate medication in the older adult population attending primary care in Portugal provided the first approach to the situation [197]. Nevertheless, data on Portuguese institutionalized older adults are lacking. Therefore, our study aimed to examine the prevalence of polypharmacy and potentially inappropriate medications in a population of older adults living in nursing homes of the city of Viseu, in central Portugal. Furthermore, we also intended to assess the possible association between polypharmacy, potentially inappropriate medications and cognitive impairment in our population of institutionalized older adults.

5.2. Material and methods

5.2.1. *Patient and Public Involvement*

Patients and the public were not involved in the design, conduct, reporting, or dissemination plans of our research.

5.2.2. *Subject Recruitment and Data Collection*

The present work is a cross-sectional study performed with data collected from 14 long term care institutions for older adults/nursing homes that agreed to collaborate in the study and are located in the city of Viseu, Portugal or within a distance of 20 km (12 min) from the city. These nursing homes represent 90% of the total nursing homes in the city and they could be either private or supported by the government. To be included in the study, these nursing homes should have more than 25 beds and be supported by health professionals (a nurse and a general practitioner). A total of 698 patients from all the nursing homes who had agreed to enroll in the study were then contacted and informed about the study. Inclusion criteria were:

(i) age ≥65 years old, (ii) residence in nursing homes at least for the past 12 weeks prior to the study, (iii) Barthel Index (BI) ≥ over or equal to 40 points, (iv) ability to walk (with or without technical devices), (v) understand written and spoken Portuguese and (vi) acceptance to participate in the study. The exclusion criteria were: (a) temporary residence in the institution or residence for <3 months prior to the study, (b) exhibit cognitive and behavioral deterioration suggesting inability to understand or give informed consent or had a diagnosis of Alzheimer's disease and (c) decline to participate in the survey. Only 193 participants met the eligibility criteria. However, six declined to participate. Figure 5.1 provides a participant inclusion flowchart.

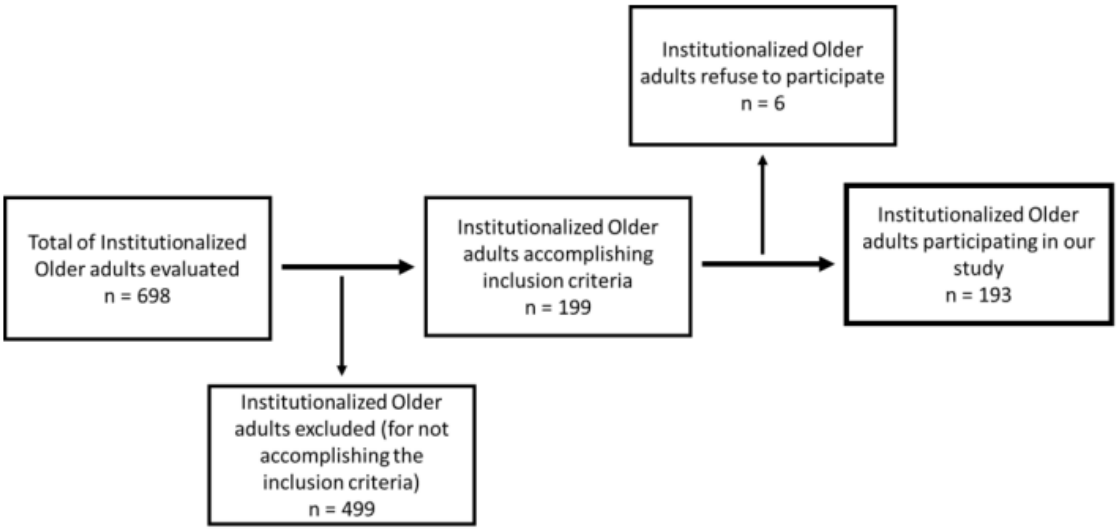

Figure 5.1. Participant inclusion flowchart.

The included institutions are residential structures for the elderly (ERPI) that have their own kitchen, so all have a cook and kitchen assistants. In addition to management positions, they also have social workers and operational assistants/home helpers who provide support to all the elderly. These institutions also have the support of social workers, physical education teachers and a health team (nurse, physiotherapist and a doctor). The study was approved by the Ethics Committee of the Polytechnic Institute of Viseu (see appendix 1) (Ref. 01/sub/2021) and conforms to the provisions of the Declaration of Helsinki (as revised in Brazil 2013). All participants gave their written informed consent to participate in the study. The reporting of this study conforms to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement [198].

Following written informed consent, a trained researcher collected the data and performed the anthropometric measures. Data was collected from September 2018 to June 2019. Data collection included demographic and socioeconomic characteristics (sex, age, educational level, marital status), functional status for instrumental activities of daily living (ADL), cognitive function and number and type of medication. The formal education demographic was categorized according to the number of school attendance years: illiterate (0 years), 1–11 years, >11 years. The information collected was recorded in a computerized database designed for this purpose. This database was anonymized prior to any analyses to ensure data protection.

5.2.3. *Body Mass Index (BMI)*

Anthropometric measurements, such as weight and height, were undertaken. Height (rounded to the nearest 0.1 cm) was measured using a measuring tape, with the participants standing upright against a wall without shoes. Participants were weighed with a digital chair scale to the nearest 0.1 kg. BMI was calculated as weight (kg)/height $(m)^2$, and classified according to Lipschitz *et al.* [48].

5.2.4. *Performance in Activity of Daily Living (ADL)*

BI is an index used to evaluate the functional ability of elderly in 10 ADL (ambulation and chair/bed transfers, bathing self, personal hygiene, stairs climbing, feeding, toilet use, bowel control, bladder control, dressing) [199]. The index is calculated by summing the response value to each of these items. It has been validated in the Portuguese population [200]. The higher the score following Barthel Index assessment, the greater the likelihood for the patient to be able to live at home, independently, with varying degrees of help and care. The BI total score ranges from 0 to 100 points and classifies the individual's level of dependence as follows: score under 20, totally dependent; score between 20 and 39, very dependent; 40 and 59, partially dependent; 60 and 79, minimally dependent; and 80 and 100, able to live independently [200].

5.2.5. *Cognitive Performance*

Cognitive status was evaluated by the Mini Mental State Evaluation (MMSE) validated for the Portuguese population [173]. This is one of the most widely used instruments for cognitive impairment screening. It includes 30 items and assesses temporal and spatial orientation, working memory, recall, attention, arithmetic capacity, linguistic, and visual-motor skills. The

maximum score is 30 points (one point per correct item). The minimum cut-off for adequate cognitive functioning is set accordingly to the level of education of the participant. In the present study, cognitive impairment was defined using the following cut-off score points: ≤15, illiterate, ≤22, 1-11years of study, and ≤27, >11 years of study [145].

5.2.6. *Polypharmacy and PIMs*

Information regarding medication was collected based on patient records provided by the nursing staff. The medicines used by the participants were classified into pharmacologic groups based on those defined on the Portuguese "Therapeutic record". Polypharmacy was divided into minor (2 to 4 daily medicines) and major (5 or more daily medicines). Considering that five or more medications should be taken regularly for a longer period of time, time-limited medications such as antibiotics were excluded from the calculation of total number of medications taken by each patient. Furthermore, supplements and vitamins that do not need a prescription (e.g., calcium, multivitamin) were also excluded. However, supplements that require a prescription such as vitamin B12 and potassium chloride were included.

For each participant, PIMs were assessed based on the Beers Criteria [100], independently of patient diagnosis or conditions once an individual's clinical history was not provided. Authors used the last updated (2019) version of the criteria released by the American Geriatric Society for Potentially Inappropriate Medication Use in Older Adults [105]. This tool has already undergone several revisions, the last being in 2019, and includes six tables: listing "potentially inappropriate medications in older patients apart from the clinical condition" Table 5.2, "medication use in older adults due to drug–disease or drug– syndrome interactions that may exacerbate the disease or syndrome" Table 5.3, "potentially inappropriate medications in older patients considering the clinical condition" Table 5.4, "potentially inappropriate medications—drugs to be used with caution in older adults" Table 5.5, "potentially clinically important drug–drug interactions that should be avoided in older adults" Table 5.6, and "medications that should be avoided or have their dosage reduced with varying levels of kidney function in older adults" listed in Table 5.7. The criteria were applied using only the information contained in the sociodemographic characteristics (age and gender) and patients' current medication list (i.e., international nonproprietary names, dosages, pharmaceutical forms, and regime of each medicine). The information of 2019 Beers Criteria Table 6 was ignored because creatinine clearance data were not available in the patients' medical records. Classification was performed by two independent authors (C.C

and E.T.L.). When discrepancies existed, a decision was achieved by consensus meetings between the authors.

5.2.7. *Statistical analysis*

Analysis of data involved descriptive statistics such as mean, standard deviation and frequencies of sociodemographic variables (continuous and categorical) such as age, gender, educational level and marital status, and BMI, BI and MMSE classes. The gender effects were analyzed by Chi square tests according to the above variables and polypharmacy and potentially inappropriate medications variables. The association between presence or absence of polypharmacy and nutritional status, functionality for daily living, cognition and the presence of potentially inappropriate medication was achieved with Chi square tests. Binary logistic regression analysis was used to understand the influence of the factors age, gender, polypharmacy, the presence of PIMs and pharmacological classes on cognitive impairment (MMSE scores). The collected data were analyzed using IBM SPSS Statistics software, version 26.0. The level of significance of $p \leq 0.05$ was considered for all statistical analyses.

5.3. Results

5.3.1. Characteristics of the Participants

A total of 193 nursing home residents were recruited, with a mean age of 82.4±6.2 years (ranging from 65 to 95 years old); 72.5% (n=140) were female participants. The participants presented a low educational level (illiterate or 11 years of schooling =88.0%) and most of them were widowed, separated or divorced (73.6%). BMI values ranged from 16.0 kg/m2 to 43.3 kg/m^2, with a mean value of 28.5±5.0 kg/m^2. Roughly 6.7% of the subjects were classified as underweight (BMI <22 kg/m^2), while 58.5% were considered overweight (BMI >27 kg/m^2). There were no significant differences by gender in the three BMI categories. For ADL, most of the population (74.6%) were able to live independently, according to their BI scores. A total of 70 participants (36.3%) presented some degree of cognitive impairment according to the MMSE screening, with women having a worse cognitive performance than men (p=0.015). Sociodemographic data as well as BMI, BI and MMSE scores are summarized in Table 5.1.

Table 5.1. Main baseline characteristics of the study population by gender (n=193).

	Total Number (%)	**Female Number (%)**	**Male Number (%)**	***p*-value**
Educational Status				
Illiterate	68 (35.2)	52 (76.5)	16 (23.5)	
1-4 years	102 (52.9)	74 (72.5)	28 (27.5)	0.350
>4 years	23 (11.9)	14 (60.9)	9 (39.1)	
Civil Status				
Single	23 (11.9)	19 (82.6)	4 (17.4)	
Married	28 (14.5)	13 (46.4)	15(53.6)	0.003*
W/S/D	142 (73.6)	108 (76.1)	34 (23.9)	
BMI				
Underweight	13 (6.8)	8 (61.5)	5 (38.5)	
Normal	67 (34.7)	49 (73.1)	18 (26.9)	0.654
Overweight	113 (58.5)	83 (73.5)	30 (26.5)	
BI				
Partially dependent	13 (6.7)	11 (84.6)	2 (15.4)	
Minimally dependent	36(18.7)	29 (80.6)	7 (19.4)	0.246
Independent	144 (74.6)	100 (69.4)	44 (30.6)	
MMSE				
Cognitive impairment	70 (36.3)	58 (82.9)	12 (17.1)	0.015*
Without cognitive impairment	123 (63.7)	82 (66.7)	41 (33.3)	

Note: W/S/D - Widow/Separated/Divorced; BMI -Body Mass Index; BI-Barthel Index; MMSE -Mini Mental State Examination. *Statistically significant differences ($p<0.05$), using the Qui-Square test.

5.3.2. Polypharmacy and PIM

The participants were found to take an average (±standard deviation) of 7.6±3.3 drugs per day. Polypharmacy was identified in 97.9% of the elderly, 80.8% of which were taking 5 or more medications per day. 79.3% of the participants presented at least one PIM (Table 5.2).

Table 5.2. Polypharmacy and Potentially Inappropriate Medications by gender.

	Total	Female	Male	*p*-value
Polypharmacy				
Minor Polymedication (2-4 drugs)	37 (19.2)	26 (70.3)	11 (29.7)	0.731
Major Polymedication (≥5 drugs)	156 (80.8)	114 (73.1)	42 (26.9)	
Potentially Inappropriate Medications				
0 drugs	40 (20.7)	25 (62.5)	15 (37.5)	
1 drug	75 (38.9)	50 (66.7)	25(33.3)	0.046*
2 drugs	52 (26.9)	44 (84.6)	8 (15.4)	
≥3 drugs	26 (13.5)	21 (80.8)	5 (19.2)	

Percentages in brackets. *Statistically significant differences (p<0,05), using the Qui-Square test.

The most commonly prescribed medications were anti-hypertensives, followed by psychiatric agents (67.4%) and other cardiovascular medications (66.3%) (Figure 5.2). Figure 5.2 also shows that other pharmacological subsets were consumed but in lower percentages.

According to the Beers Criteria, the pharmacological groups of most found PIMs were short-acting benzodiazepines (alprazolam) (46.6%) and proton-pump inhibitors (omeprazole) (43.5%) (Figure 5.3). Moreover, long-acting benzodiazepines (diazepam) and antipsychotics such as quetiapine, loxapine, and haloperidol (in descending order) were found. Table 5.3 presents information on the magnitude of associations between polypharmacy and the different health domains analyzed as well as the presence of PIMs. Our analysis revealed a significant association between major polypharmacy and cognitive impairment (p=0.039). However, functionality for basic daily living activities (BI) does not seem to be affected by polypharmacy in this group. Major polypharmacy and PIM were significantly associated (p<0.001) (Table 5.3).

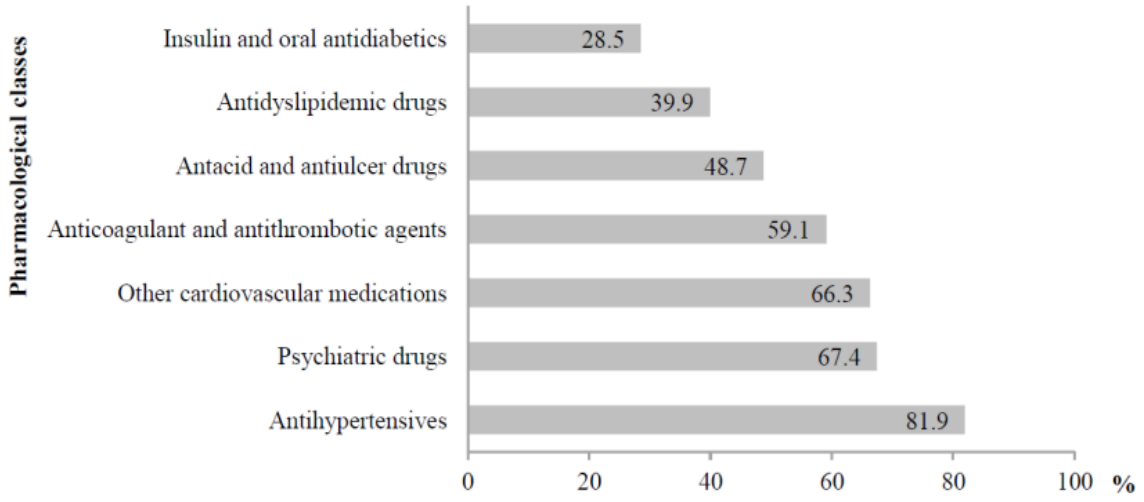

Figure 5.2. Drug classes most frequently used by the participants of the study (%).

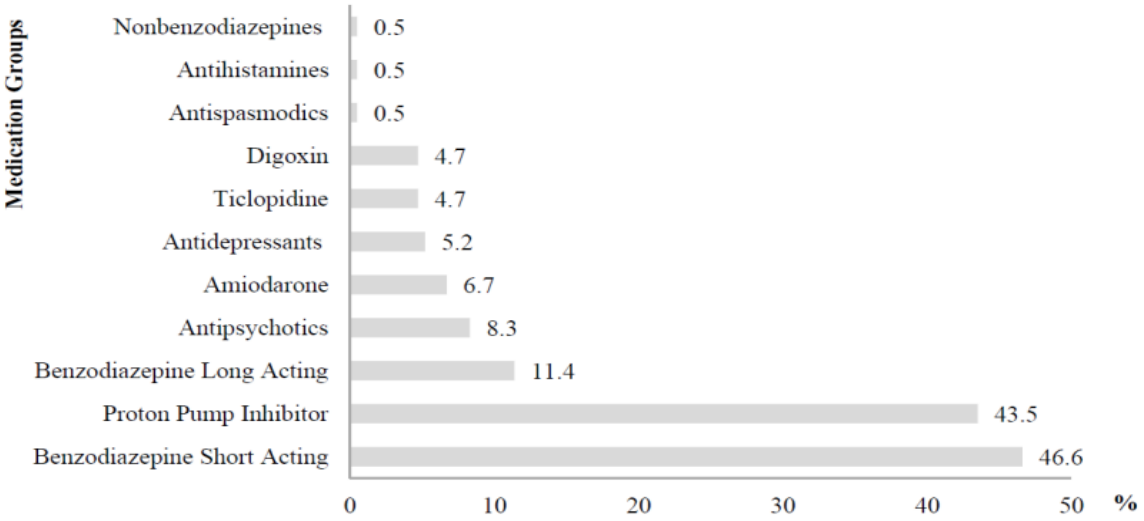

Figure 5.3. Therapeutic classes and drugs to be avoided for most older adults according to the Beers Criteria (independent of diagnoses or conditions).

To understand the possible association between cognitive impairment (as measured by MMSE scores) and several factors such as age, gender, polypharmacy and the use of some drug classes, binary logistic regression analysis was performed (Table 5.4). In our population, female participants had a higher likelihood of having cognitive impairment than their male counterparts (p=0.017). Similarly, patients taking five or more prescription drugs per day (major polypharmacy) or consuming any psychiatric, gastrointestinal or oral antidiabetic agents (regardless of whether they were considered potentially inappropriate or not) had higher odds of displaying cognitive impairment than those who did not.

Table 5.3. Association between *Major* Polymedication and Other Variables.

	Presence of Major Polymedication Number (%)		
	No	Yes	***p*-value**
Age			
65-76	11 (26.8)	30 (73.2)	
77-86	17 (17.0)	83 (83.0)	0.373
87-99	9 (17.3)	43 (82.7)	
Gender			
Female	26 (18.6)	114 (81.4)	0.731
Male	11 (20.8)	42 (79.2)	
BMI			
Underweight	3 (23.1)	10 (76.9)	
Normal	19 (28.4)	48 (71.6)	0.043*
Overweight	15 (13.3)	98 (86.7)	
BI			
Partially dependent	1(7.7)	12 (92.3)	
Minimally dependent	4 (11.1)	32 (88.9)	0.176
Independent	32 (22.2)	112(77.8)	
MMSE			
Cognitive impairment	8 (11.4)	62 (88.6)	0.039*
Without cognitive impairment	29 (23.6)	94 (76.4)	
PMI			
No	23 (57.5)	17 (42.5)	0.000*
Yes	14 (9.2)	139 (90.8)	

BMI—body mass index; BI—Barthel Index; MMSE—Mini Mental State Examination; PIM—potentially inappropriate medication. Illiterate individuals with MMSE score ≤15, individuals with 1 to 11 years of study and MMSE score ≤22 and individuals with more than 11 years of study and MMSE score ≤27 were considered to have cognitive impairment. N = number of patients. Percentages in brackets. Statistical comparisons between older adults with major polypharmacy (≥5 drugs) or without polypharmacy by Chi square. * Statistically significant differences ($p<0.05$).

Table 5.4. Binary logistic regression analysis of potential association between cognitive impairment (MMSE scores) and the factors age, gender, major polypharmacy, PIM and various pharmacological classes in institutionalized older adults.

	OR	CI 95%	*p*-value
Age	1.000	0.954-1.049	1.000
Male	0.414	0.200-0.855	0.017*
Female	2.417	1.169-4.994	0.017*
Major Polymedication	2.391	1.026-5.571	0.043*
Presence of PIM	0.823	0.440-1.537	0.019*
Antihypertensives	1.300	0.594-2.845	0.511
Psychiatric medication	2.347	1.193-4.614	0.013*
Other Cardiovascular Medication	0.958	0.516-1.781	0.893
Anticoagulant and Antithrombotic Agents	1.062	0.584-1.932	0.842
Antacid and Antiulcer Drugs	1.867	1.030-3.384	0.040*
Antidyslipidemic Agents	0.567	0.306-1.050	0.071
Oral Antidiabetics	2.060	1.017-4.173	0.045*

OR – Odd Ratios; CI – Confidence intervals. *Statistically significant correlations ($p<0.05$).

5.4. Discussion

Polypharmacy and PIM is a paramount concern all over the world [201,202]. Institutionalization and cognitive decline seem to be predictive risk factors for these conditions [203,204]. It is estimated that approximately 60-70% of long-term home-care residents have some degree of cognitive impairment [205,206] and that within this population more than 20% take 5 or more medications [133,207]. It is noteworthy that a high prevalence of PIM has been reported among patients with dementia, including Alzheimer's disease [208]. To the best of our knowledge, this is the first study performed in nursing homes of the city of Viseu, in central Portugal, reporting the prevalence of polypharmacy and PIM and their possible association with cognitive impairment in a population of older adults.

Our study identified major polypharmacy (five or more drugs) in 80.8% of the studied nursing home older adults, 79.3% of whom used at least one PIM. The number of consumed drugs per day is different among nursing home residents across countries. Different physicians' attitudes when prescribing treatments for complex patients may explain such differences [208,209]. On average, the number of daily medications described in this study accorded with the SHELTER project data obtained across 57 institutions from eight different European countries (7.0±3.6, average (SD)) [205]. Our results pointed out a significant risk factor for receiving inappropriate drugs when major polypharmacy occurs, especially in women. Our

study adopted the most updated Beers Criteria, which allows the identification of drug inappropriateness in the older adult population. The Beers Criteria are a practical tool for screening potential drug-related problems and to guide drug prescription in different health care settings. Short-acting benzodiazepines were the principal PIM consumed by the participants, followed by proton-pump inhibitors. Previous studies had highlighted the same inappropriate exposure to benzodiazepines in institutionalized older adults, with rates reaching 30% [192,210]. Benzodiazepines seem to be widely used by Portuguese older adults. Nevertheless, their use is often inappropriate and calls for concern. They are used for the treatment of insomnia and anxiety, and their consumption is often related with decreased cognitive impairment [211,212] and the high rate of falls and hip fracture [213]. The present study included institutions considered as residential structures for the elderly (ERPI), welcoming from completely autonomous elderly people to elderly people with various types of physical dependence. Here, older adults benefit from the intervention of multidisciplinary technical teams. All have a nursing team integrated into the technical staff of the institution and also have the support of a general practitioner who visits the institutions regularly. The design of these structures may partially justify the elevated presence of independent older adults in ADL (74.6%) with no impaired cognition (63.7%). Importantly, cognitive impairment was associated with an increased rate of major polypharmacy. A survey across community-dwelling older adults in Japan also showed a similar association, where polypharmacy was present in 48.3% of individuals with deficits in cognition [214]. Moreover, as well as in our investigation, polypharmacy was associated with decreased MMSE scores and an increased risk of cognitive impairment in other studies [133,207,215]. In fact, by increasing the number of prescribed medicines, the risk of unexpected events is increased, and cognitive function may be impacted [99]. Additionally, our results showed that elders who took at least one PIM were more likely to have lower MMSE scores. This fact is extremely important as some PIM may adversely affect cognition. Such cases should be closely followed up in order to understand whether their cognitive deficits are a consequence of neurodegenerative processes or were caused (or worsened) by any PIM [216–218]. On the other hand, the intake of these drugs helps to control neuropsychiatric symptoms, delirium episodes, aggressive behavior, and agitation, conferring protection to both the patient and the caregiver. Thus, whether categorized as PIM or not, our older adults with cognitive decline were more likely to use psychotropic medicines, oral antidiabetics, antacid, and antiulcer medicines. Longitudinal studies should be further implemented to assess the impact of PIM in the cognitive function of older adults. Additionally, a more detailed stratification of MMSE scores

and inclusion of participants with psychiatric diseases and dementia will lead to demonstration of a more accurate relationship among these variables. In fact, determining the causality/effect of cognitive function versus PIM will be essential to scrutinize whether cognitive function is affected by using PIMs, especially medications that affect cognition, or if patients with cognitive impairment and other comorbidities have the real need of more medication use and more PIM. This study highlights the importance of the involvement of a pharmacist as part of the multidisciplinary health care team in nursing homes. Pharmacists are in a unique position to close monitoring of the number of medicines prescribed to older adults, as well as their suitability. Several systematic reviews have examined the effects of pharmacist led interventions in nursing homes and have demonstrated promising results [219,220]. Considering the above results, embedding a pharmacist as part of the multidisciplinary health care team to conduct medication management activities alongside nurses, careers and doctors would be important to improve the wellbeing of older adults in nursing homes [221]. Our study had some limitations. First, the small sample size. Then, the cross-sectional design of our study, besides not allowing extrapolation to big populations, only collects the data at a single moment in time. In this way, it was not possible to assess PIMs when they are only considered inappropriate when used for more than a specific period. The Beers Criteria can only identify potentially inappropriate medications, not actually inappropriate medications. In addition, in the design of the study, the inclusion criteria were established to minimize the impact on the elder. Highly dependent individuals in which anthropometric measures are difficult to perform were excluded as well as those with cognitive impairment in which external interventions may disturb and condition their normal routines. Thus, these implemented inclusion criteria might reduce some correlation strength. Nevertheless, this study characterized multiple indexes of older adults (BI for ADLs, MMSE for cognitive impairment and BMI for nutritional status), allowing a complete and integrated vision of the studied population.

5.5. Conclusions

Our investigation expands the knowledge on polypharmacy and the use of PIMs and their attendant risk for the cognitive status of institutionalized older adults in Portugal, where data in this field are scarce. This study found a population with reduced prevalence of cognitive and functional disability but with a very high incidence of polypharmacy and PIM. We believe that this finding will serve to alert health professionals (doctors, pharmacists, nurses) of the need to regularly and methodically control the prescriptions of older adults. In addition, non-pharmacological interventions should be considered in order to improve or maintain functionality and cognition in institutionalized older adults. The prevalence of polypharmacy and PIM may increase the likelihood of cognitive impairment. Thus, minimizing and preventing these situations perhaps may be beneficial to the cognitive function of older adults. Reducing polypharmacy in addition to disease control may delay the harmful effects on cognition induced by age and, therefore, this study also reinforces the value of constant verification of both polypharmacy and PIM in older adults with cognitive impairment. Overall, this study aims to shed light and increase awareness of the importance of polymedication and PIM among older adults, with inherent implications for policy makers.

Chapter 6 | General Discussion

Population aging is an increasing and complex challenge that modern societies need to face. Due to changes in sociocultural dynamics, institutionalization of elderly relatives is increasingly frequent. Therefore, strong strategies and methodologies to promote *Active Aging* should be validated and translated into tangible improvements to the quality of life for the elderly.

In older adults, nutritional status is a challenging health concern. Aging has inevitable physiological changes that contribute to a decrease in appetite in addition to a decrease in nutrient absorption, both hindering the maintenance of an adequate nutritional status. The assessment of nutritional status and dietary intake of seniors, in particular those in nursing homes, are essential tools to prevent increase of comorbidities and the decreasing functional and cognitive abilities.

In this study, the reality of nursing homes in the municipality of Viseu was addressed. This Portuguese region has one of the highest aging indexes in the country. In the analyzed sample, female individuals were the most representative which reflects the global demographic trend according to WHO data. Moreover, for 2019 data, PORDATA indicates a higher life expectancy for females (83.7 years) when compared to males (78.1 years) [222]. The mean age of the older adults was 82 years old (between 65 and 95 years old) which is in line with the average life expectancy for the population (81.1 years in 2019). The institutionalized seniors also present a higher incidence of low literacy with approximately 95% having less than 11 years of education or illiterate. Concomitantly, up to 70% of nursing home residents were divorced, single or widowed. Overall, these characteristics were observed in other Portuguese studies with institutionalized individuals [146,147].

Different screening tools might be used to evaluate nutritional status and their corresponding risks. Among them, we emphasize the MNA. This tool has easy application and low cost and it has been widely used by researchers and practitioners. Nutritional assessment might also be performed using BMI, some skinfold measurements, mid harm circumferences and also biometric impedance analysis. BMI predicts disease risk in those who are obese and in those termed underweight. Measurement of BMI in older people has certain limits associated with the loss of height caused by aging. Moreover, in the presence of factors such as ascites and edema BMI can be unreliable. In addition, unintentional weight loss is not identified by a single determination.

The prevalence of overweight (BMI ≥27 kg/m^2), based on Lipschitz [48] classification was 57.9% (72.6% women *vs* 27.4% men). These obtained values cannot be compared with others, because cut off points were different from those of OMS for adults. Specific cut-offs for this age group are still not consensual. The choice of Lipschitz [48] classification was taken in consideration because of the mean age of the participants, changes in body composition and fat distribution due to aging. These criteria were not considered in WHO classification. The impact of obesity on health outcomes in older people is complex and not completely understood. Several studies [223,224] demonstrated that the BMI range associated with lowest mortality was higher for older adults (e.g., 27 – 30 kg/m^2 for men, 30 – 35 kg/m^2 for women). Therefore, in order to interpret BMI findings as the ones reported in the present study, the definition of excess weight and its health consequences in older ages requires further research.

Too often, research including nutritional assessments ignores the complexity of nutritional status of older adults and uses a single parameter such as the low body mass index. Early detection of those at risk of becoming malnourished is particularly important in older adults, namely multi-morbid adults. Screening tools for malnutrition are generally of questionnaire format, addressing risk factors for malnutrition (e.g., functional limitations or poor appetite), and indicators of malnutrition (e.g., involuntary weight loss) [225]. In order to evaluate the nutritional risk of the participants we additionally used the MNA short form, validated for the Portuguese population.

Considering MNA results, higher frequencies of risk of malnutrition were observed in other studies conducted in Europe (42% in Germany, 51% in Spain, 46% in Italy) as compared to 28.0% in our study [185–187]. These discordances may be related to participants' characteristics. For example, those expected to have a worse nutritional status, such as older adults with dementia, bedridden or not able to understand the informed consent, were not assessed in this study.

Analyzing the results obtained for nutritional status and nutritional risk, the percentage of incorrect malnutrition (under or overweight) found by BMI was far superior to that identified by the MNA (~ 65% versus 28%). Considering all the above, although it is a simple and cheap method, BMI does not reflect changes in body composition which are inherent to the aging process. By opposition, MNA includes information about muscle mass (leg and arm perimeter), weight loss, food intake (consumption of specific food groups and liquids, number of meals, autonomy in eating), health status (medication, lifestyle, mobility, presence of acute stress and presence of dementias) and subjective information (self-perception of health)

assessed through questions that can help to determine from form the state of malnutrition more completely. These MNA characteristics may increase sensitivity when compared with anthropometric measures. On the other hand, as MNA scores are more focused on identifying malnutrition in terms of undernourishment, their results might underestimate the other extreme of malnutrition, obesity. All obesity cases are included in the group of well-nourished as both normal and obese group share the same MNA score (25.0±2.0 and 25.3±2.2) (see table 4.3, Chapter 4). These data similarity may difficult the necessary interventions to combat obesity.

Despite the particularities attributed to each nutritional assessment tool, a close relationship was found between anthropometric values (BMI and WC) and MNA scores. A positive correlation was observed between BMI and WC and nutritional risk; however, statistical significance was only achieved between BMI and MNA score, despite this correlation not being very strong. Nevertheless, the measurement of waist circumference might be adopted as a routine measurement in clinical practice alongside BMI to classify obesity.

This study has shown that participants had high intakes of total fat, carbohydrate and salt and low intakes of dietary fiber and micronutrients, such as vitamin B12, D and E, calcium and magnesium. Women were more prone to present deficiency than men. Moreover, this population presented inadequate ingestion of protein (75.2%), fat (30.3%) and carbohydrate (33.2%). In addition, our results showed that elderly at risk of malnutrition presented inappropriate energy and nutrient intakes when compared to those with a normal nutritional status. This relationship has been already demonstrated by Ongan and Rakicioğlu [140] and Vikstedt *et al.* [67]. According to the classes of MNA, women presented more significant statistical differences than men in macro and micronutrients, suggesting that women seem to be particularly vulnerable. High percentages of residents in nursing homes have an intake of less fiber, vitamin E, vitamin D, iron, iodine, and folic acid when compared to the recommended values [67,70]. A recent systematic review which examined 28 studies including 2036 older adults (≥60) living in institutions in seven Western countries identified consistent nutritional insufficiency [226]. Different causes may be attributed to inadequate food consumption such as lower dairy products intake [227]. On the other hand, and according to have been observed in the general European population, we observed a high prevalence of sodium inadequacy, which is associated with cardiovascular events and mortality [118,152]. These findings stress the importance of adequate food consumption and nutritional screening of institutionalized elderly, reinforcing the need to develop interventions and maintain adequate nutritional status by slowing down the process leading to malnutrition.

Our systematic review (see Chapter 2) also validates an adequate nutritional status as an important parameter in preventing cognitive and functional decline in institutionalized elderly. However, scarce information exists regarding these relationships in institutionalized senior adults. In this study, cognitive and functional abilities were also assessed in nursing home residents, showing a moderate vulnerability with minimal dependence on ADL (69.6%) and impaired cognition (39.3%) (see Chapter 4). Our work was able to validate the nutritional status impact on the ability to perform ADL and cognitive functions in institutionalized older adults, showing a positive correlation between MNA and BI ($r=0.4$, $p<0.0001$), and a slightly positive correlation between MNA and MMSE ($r=0.3$, $p<0.0001$). In general, well-nourished individuals perform better in ADL. Other studies had already demonstrated a similar relationship between malnutrition and functional dependence [188]. Furthermore, elderly at risk of malnutrition presented significantly increase in cognitive impairment compared to the well-nourished, showing that cognitive and functional abilities were interconnected.

Other factor that affects elderly, is the fact that, with age, the number of medications taken also increase. We found that the studied elderly population took an average of 7.6±3.3 drugs per day with a minimum of 0 and a maximum of 12 daily drugs. Polypharmacy was identified in 97.9% of the elderly, 80.8% of which were taking 5 or more medications per day (Chapter 5).

In order to face multiple pathologies, polymedication is a reality, both in our study and in other similar ones, as well as in elderly in general. Nevertheless, it should be highlighted that excessive medication is also associated to increased loss of appetite, change in bowel function and modification of some metabolic processes, being able to directly condition the nutritional status of the individual [63].

The most commonly prescribed medications identified in our study were anti-hypertensives, followed by psychiatric (67.4%) and cardiovascular medications (66.3%) (see Chapter 5). In fact, these classes of medicines are the most commonly associated with geriatric syndromes such as cardiovascular diseases, asthma and mental health conditions [228].

Assessing the prescribed drugs, according to Beers criteria, 79.3% of the studied seniors presented at least one PIM. Short-acting benzodiazepines (46.6%) and proton pump inhibitors (43.5%) were the most prescribed ones (see Figure 5.3, Chapter 5).

Female participants were more prone to have at least one PIM as well as to suffer from cognitive impairment. We also found that elderly who took more than five prescription medicines per day (major polypharmacy), or consuming any psychiatric, gastrointestinal or

oral antidiabetic agents (regardless of whether they were considered potentially inappropriate or not) had higher odds of displaying cognitive impairment than those who did not.

The constant introduction of new therapeutic guidelines and the increase in character treatment preventive measures also converge to the increase of polymedication in the elderly. In this regard, most of the existing evidence concerning this type of population comes from observational studies, excluding the elderly population that participate in clinical trials. Undervaluation of some characteristics such as multiple pathologies gives rise to inconsistencies that hampering the extrapolation of the obtained results to a heterogeneous population like is the elderly.

Chapter 7 | General Conclusions

In the present study, the assessment of nutritional status and dietary intake of nursing home residents in the municipality of Viseu was made. In that sense, it can be stated that:

- Nutritional status and dietary balance of elderly are essential conditions to support general health and to improve Quality of Life (QoL);
- The risk of malnutrition is related to a greater functional dependence, as well as to cognitive impairments;
- Given the vulnerability of the institutionalized elderly, it's important the classification of its nutritional status based on both BMI and MNA;
- MNA has been proven to be an accurate and easily implemented method to identify malnutrition as it combines several factors such as height, modification of the body composition, disease status and self-perception of health;
- Energy intake is inversely associated with malnutrition;
- Inadequate intakes were found for all macronutrients, special focus in protein with a 75.2% of elderly with inadequate protein intake;
- Elderly at risk of malnutrition presented inappropriate energy and nutrient intakes when compared to those with a normal nutritional status;
- Older adults are at an increased risk of micronutrient deficiencies and its correction with food supplements are often need;
- Regarding medication of older adults, the present study is a contribution for the scarce data in this field, at least in Portugal, showing a very high incidence of polypharmacy and PIMs;
- Minimizing and preventing the prevalence of polypharmacy and PIMs can be beneficial to reduce cognitive impairments induced by age, shedding light and increasing awareness of the importance of polymedication and PIMs on elderly, with inherent implications for policy makers.

Thus, according the previous statements, it can be concluded that:

- Appropriate nutritional status and dietary nutritional management in nursing home residents are essential to preserve their health and quality of life;
- Since nutritional status can be adjusted and has been reported to have very intricate links to cognition, independence and autonomy, a closer evaluation of nutritional

status on these parameters is crucial to prevent associated health issues in the elderly population, especially the one that lives in nursing homes;

- Non-pharmacological interventions should be considered, namely the implementation of cognitive and motor stimulation programs, as well as interventions aimed to achieve a correct diet, in order to reach higher levels of independence and autonomy, allowing to an improvement in self-care and overall well-being of elderly;
- A global strategy to control the disturbances of well-being should include regular and individualized malnutrition risk assessment, early diagnosis of malnutrition, identification of patients who may benefit from nutritional support, identification and treatment of nutritional deficiencies, determination of nutritional needs and control of treatment effectiveness.

7.1. Future perspetives

The present thesis, done in Viseu, demonstrated that much work remains to be done about elderly, particularly nursing home residents.

To complement this study, it would be interesting to find if the group of older people became malnourished, before or after institutionalization, in order to better define targeted interventions and public health strategies for seniors.

On other hand, given the inadequate nutrient intakes found in our study, it would be pertinent to discuss the use of food supplements in these institutionalized elderlies, in order to correct/improve the outcomes that were presented above.

Another interesting goal would be to study the link between mortality, nutritional status and dietary intake of the studied population to ascertain the relevance of the referred results considering prospective survival data and the individual baseline characteristics.

In addition, the use of multiple assessment tool for either nutritional status, dietary intake or even cognitive and functional abilities can in future help to design specific diagnostic measures to improve senior quality of life.

Last but not least, a larger study should be implemented in different Portuguese districts in order to confirm (or not) the data obtained in Viseu. The proposed study should include a complete representation of institutionalized Portuguese senior population, highlighting geographic differences and differentially evaluate nutritional, cognitive and functional status in Portuguese older adults.

Finally, this study, by characterizing and highlighting the needs of Portuguese institutionalized older adults in Viseu, can be considered a small contribution to the recent creation of the Multidisciplinary Institute of Ageing of the University of Coimbra of which the Faculty of Pharmacy is a part of.

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Appendix 1. Study approval by the Ethics Committee of Polytechnic Institute of Viseu

Politécnico de Viseu 40 anos

Formulário para Avaliação Ética de Estudos: Comissão de Ética do Instituto Politécnico de Viseu (IPV)

Formulário para Avaliação Ética de Estudos de Investigação

Título do projeto	Polimedicação, medicação potencialmente inapropriada e suas possíveis implicações nutricionais, funcionais e cognitivas: Estudo numa população de idosos institucionalizados
Proponentes do projeto	Jorge Oliveira Catarina Caçador João Páscoa Pinheiro Fernando Ramos
Investigador responsável	Prof.ª Doutora Edite Teixeira de Lemos
Parceiros do projeto	Escola Superior Agrária de Viseu, Instituto Politécnico de Viseu e CERNAS-IPV Centro de Investigação Faculdade de Farmácia Universidade de Coimbra Faculdade de Medicina da Universidade de Coimbra REQUIMTE/LAQV, Faculdade de Farmácia, Universidade de Coimbra
Data de submissão	15/01/2021
Relator(es)	Ernestina Maria V Batoca Silva Joana Raquel Fernandes Quina Araújo Carlos Manuel Baptista Fiolhais
Data da aprovação do parecer	22/01/2021
A presidente da CE	Ernestina Batoca Silva

PARECER N.º 01/SUB/2021

X	**PARECER ÉTICO FAVORÁVEL** (A proposta é eticamente aceitável)	**MOTIVOS:**
	PARECER ÉTICO FAVORÁVEL COM RECOMENDAÇÕES (sujeito ao cumprimento de requisitos éticos e recomendações)	**MOTIVOS:** ***(Ver requisitos e recomendações)***
	PARECER ÉTICO NÃO FAVORÁVEL	**MOTIVOS:**