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Nutrients associated with diseases related to aging: a new healthy aging diet index for elderly population

Nutrientes asociados a las enfermedades relacionadas con el envejecimiento: Un nuevo índice de dieta saludable para personas mayores

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Received: 01/04/2018

Accepted: 10/06/2018

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DOI: 10.20960/nh.1946

Authorship declaration: Manuel Lozano and José María Ramada designed the research; Manuel Lozano and Lara Manyes conducted the research; Juanjo Peiró analyzed the data; and Manuel Lozano, Lara Manyes, Juanjo Peiró, and José María Ramada wrote the paper. José María Ramada had primary responsibility for the final content. All authors read and approved the final manuscript.

ABSTRACT

Introduction: several indexes are used to measure the quality of nutrition in advanced ages. None of them were designed to evaluate nutrition to avoid disabilities in elderly population.

Objectives: to retrieve from literature “nutrients and intakes” showing to be involved in aging, and propose a new index, considering this information, to evaluate the quality of nutrition for preventing diseases related to aging.

Methods: a bibliographic review was performed, retrieving information on nutrients associated with aging. All these nutrients were incorporated into a new Healthy Aging Diet Index (HADI). Next, a cross-sectional study was carried out with two convenience samples of elderly, collecting the nutritional and dietary data, calculating different validated indexes and comparing them with HADI to validate the results.

Results: forty-eight manuscripts were retrieved for full-text analysis. Associations were found between cardiovascular diseases and macronutrients, dietary fibre, sodium and vitamin D; cancer and fatty acids; diabetes and fatty acids, fibre and simple sugars; osteopenia/osteoporosis and calcium and vitamin D; sarcopenia and proteins, calcium, and vitamin D; and between cognitive impairment and fatty acids and folates. Sample 2, associated with rural areas, obtained lower indexes' scores. The behavior of HADI is similar to the other indexes (6.24/14 and 6.10/14 in samples 1 and 2, respectively).

Conclusions: the presented collection of nutrients adds useful evidence for the design of diets that allow healthy aging. The new index proposed is a tool of specific nutritional measurement in studies aimed to prevent diseases related to aging.

Key words: Dietary habits. Functionally-impaired elderly. Healthy aging. Nutrients. Nutrition assessment. Nutrition indexes. Nutritional requirements.

RESUMEN

Introducción: Suelen usarse diversos índices dietéticos para medir la calidad de la nutrición en edades avanzadas. Sin embargo, ninguno de ellos fue diseñado para evaluar la nutrición con el objetivo de evitar discapacidades en la población anciana.

Objetivos: Identificar en la literatura científica los "nutrientes e ingestas" involucrados en el envejecimiento, así como proponer un nuevo índice, considerando esta información, que sirva para evaluar la calidad de la nutrición con objeto de prevenir enfermedades relacionadas con el envejecimiento.

Métodos: Se realizó una revisión bibliográfica, obteniendo información sobre los nutrientes asociados con el envejecimiento. Todos estos nutrientes fueron considerados en el diseño de un nuevo Índice de Dieta de Envejecimiento Saludable (HADI). A continuación, se realizó un estudio transversal con dos muestras de ancianos (muestreo de conveniencia), recogiendo datos nutricionales y dietéticos, calculando las puntuaciones de diferentes índices dietéticos validados y comparándolos con HADI para validar los resultados.

Resultados: Cuarenta y ocho manuscritos fueron finalmente utilizados para el análisis de texto completo. Se encontraron asociaciones entre enfermedades cardiovasculares y macronutrientes, fibra dietética, sodio y vitamina D; cáncer y ácidos grasos; diabetes y ácidos grasos, fibra y azúcares simples; osteopenia/osteoporosis y calcio y vitamina D; sarcopenia y proteínas, calcio y vitamina D; y entre el deterioro cognitivo y los ácidos grasos y los folatos. La muestra 2, asociada a áreas rurales, obtuvo puntuaciones en los índices más bajas. El comportamiento de HADI es similar al de los otros índices (6.24/14 y 6.10/14 en las muestras 1 y 2, respectivamente).

Conclusiones: La recopilación de nutrientes presentada agrega evidencia científica útil para el diseño de dietas que faciliten un envejecimiento saludable. El nuevo índice propuesto es una herramienta de medición nutricional específica en estudios dirigidos a prevenir enfermedades relacionadas con el envejecimiento.

Palabras clave: hábitos dietéticos, ancianos con discapacidades funcionales, envejecimiento saludable, nutrientes, evaluación nutricional, índices nutricionales, requisitos nutricionales.

INTRODUCTION

According to the World Health Organization (WHO), healthy ageing refers to an individual's capacity to do the things that are important to the person. Healthy ageing is the process of developing and maintaining the functional ability that enables well-being in older age (1). The healthy aging concept has widely developed as the set of biological conditions and behaviors involved in an appropriate lifestyle aimed at improving well-being and life expectancy without disabilities (2,3), and there is quite evidence that shows that nutrition is relevant among these factors (4). In fact, the role of nutrition in the prevention and treatment of age-related diseases and disabilities has been highlighted by the European Union (5), which associates nutrition with a set of diseases related to pathological aging:

cardiovascular disease, cancer, diabetes, osteoporosis, sarcopenia and cognitive impairment/decline. In consequence, nutrition has also been associated with independence, well-being and safety of life due to its incidence in functional limitations (6-11).

Several indexes have been used to measure the quality of nutrition in advanced ages. Most of them are derived from the Diet Quality Score (DQI), the Alternative Healthy Eating Index (AHEI), the Mediterranean Diet Score (MDS) or the Healthy Diet Indicator (HDI), which have been explained in an extensive revision carried out by Gil et al. in 2015 (12). These indexes are frequently designed to be applied to any segment of the population based on overall healthy intakes, usually assumed in research (13). The AHEI, HDI and DQI measure the adequacy of nutrients and diet. They were designed on the basis of a general healthy diet, considering nutrients and food servings, to relate diet with chronic diseases (AHEI) or with mortality (HDI and DQI). The MDSmod measures the adherence to the Mediterranean diet, widely considered as a healthy dietary pattern. Each index has been designed according to a different rank score, indicating that the higher the score the better the score is, except in the DQI, where the ratio is inverse. None of these validated existing indexes was originally designed to evaluate nutrition in order to avoid pathological aging in the elderly population. There is a wide literature that relates specific nutrients, combinations of them, or specific daily intakes to prevention of chronic diseases and functional limitations. Further quality research is needed to compile these nutrients, and as far as we know, there is no validated index in the literature for measuring the quality of nutrition aimed to prevent pathological aging. Therefore, the objectives of this study were: a) to retrieve from the scientific literature the nutrients and intakes that have shown to be involved in the healthy aging; and b) to propose a new index, considering these nutrients and intakes, to evaluate the quality of nutrition in relation to a healthy aging.

MATERIALS AND METHODS

To identify the nutrients that influence healthy aging, an exhaustive bibliographic review was carried out to retrieve the available information on the nutrients associated with healthy aging. For all the nutrients, the syntaxes were elaborated combining the name of the nutrient with different factors involved in the aging process, using the terms *aging*, *diet*, *nutrition*, *elder*, *elderly*, *lifestyle* and *disability*, and six groups of diseases associated with pathological aging according to the literature (5): *cardiovascular disease*, *cancer*, *diabetes*,

osteoporosis, sarcopenia (loss of muscle mass), cognitive impairment and cognitive decline. The search was carried out in the databases Medline, PubMed, Embase, CAB Abstracts, CINAHL, Scopus, JSTOR, Web of Science and Google Scholar.

Only original articles and bibliographic reviews published between 2000 and 2017, written in Spanish, English and Portuguese, which analyzed the association between a nutrient and its effects on aging and the diseases associated with it were included. Initially, a total of 206 articles were retrieved, and after eliminating the repetitions, 161 articles were left to proceed with the selection process.

Each article was reviewed independently by two expert nutrition researchers (ML and LM), making a selection of the articles of interest that met the inclusion criteria. Those articles showing a disagreement between the two reviewers on compliance with the inclusion criteria were evaluated by a third expert nutrition researcher (JMR) who decided if the article was finally included in the review.

The selection of articles was carried out in three stages. In the first stage the articles were selected based on the reading of the title (in this first stage a total of 73 articles were excluded). In a second stage, the articles were selected based on the content of the abstract (in this stage, 29 articles were excluded). In a final stage the articles were selected based on the in-depth analysis of the full text of the article (in this stage eleven articles were eliminated). It was verified that the articles excluded in the last stage did not meet the inclusion criteria of the bibliographic review.

To achieve the second objective, it was necessary to compile the nutritional and dietary data of two convenience samples of elderly people to compare and validate the results. Non-institutionalized elderly people were chosen as target population. Hence, two convenience samples were recruited among users of the public social welfare services offered in the eastern region of Spain. People of both sexes, aged 65 and over, were included. Only those with a lack of cognitive ability to follow an interview were excluded. Thus, up to 469 potential participants were recruited although all questionnaires with missing data were dismissed, so finally 354 participants were included.

Participants of the first sample ($n = 203$) were residents of four metropolitan municipalities (with populations between 20,000 and 70,000 people). Participants of the second sample ($n = 151$) were residents of eleven rural municipalities of inland regions (with populations between 500 and 5,000 people).

Data on dietary intake, dietary habits, anthropometrics and demographics were collected from all participants through interviews. The interviews were carried out by social workers from each collaborating municipality, previously trained by the project managers at University. Data on food consumption were obtained in strict spring season to guarantee the same food seasonality. The PREDIMED validated food-frequency questionnaire was used (14). To verify the quality of the diet, data obtained through questionnaires were analyzed by the DIAL software, version 2.12. The daily intake of energy, macronutrients, micronutrients, alcohol and water of each participant was calculated.

The protocol of this study was approved by the Ethics Committee of (removed for blind peer review) and respects all the principles of the Declaration of Helsinki and the Spanish legal regulations on protection of personal data. Study participants were informed of the objectives and the scope of the study and signed an informed consent for their participation. Nutritional and dietary data obtained from the study sample were used to calculate the scores of four nutritional indexes already validated: MDSmod, AHEI, HDI, and DQI, as well as the proposed new Healthy Aging Diet Index (HADI).

The procedure followed to select the nutrients to be considered in the new HADI was carried out in two stages: a) in the first place, the six groups of diseases most frequently associated with pathological aging were chosen, according to the literature (cardiovascular disease, cancer, diabetes, osteoporosis, sarcopenia and cognitive impairment/decline) (5); and b) next, from the group of nutrients found in the literature review, those that were significantly associated to these six groups of diseases were selected to be reflected in the HADI, also considering the dietary pattern followed by the population samples of this study (15).

Likewise, the total intake of liquids was added to the design of the HADI due to its well-known effect on the general state of health in elderly people and its relevance in dehydration.

Additionally, optimum daily consumption ranges were considered according to the recommendations made in the literature (15-19). The score was applied following the methodology used in the validated indexes (12), based on the discretization. Thus, the participant obtains 1 point if the average intake of nutrients meets the criterion, and 0 if it does not comply.

The “optimal score” was defined as the maximum score that can be obtained with the application of the HADI and its value is 14. The closer the score of the maximum score is, the better the quality of the diet in relation to a healthy aging.

Thus, mean scores of each index were calculated in both samples to assess the suitability of the nutritional pattern and to evaluate possible differences in both samples. See Gil et al., 2015 (12) for design details as well as the methods to obtain the scores in each validated index.

The result of each index was presented as scores (two decimals) and also as a percentage (one decimal) of the maximum score established for each index to compare the scores obtained with these four indexes and the new index proposed in this study (HADI).

The Student’s t-test was performed among samples to verify the estimates of the indexes (p -value > 0.05 indicates equivalence between samples). All statistical analyses were performed using R version 3.2.4.

The STROBE guidelines for observational studies have been followed in this study.

RESULTS

Figure 1 summarizes the articles retrieved in the bibliographic review carried out to identify the nutrients involved in healthy aging. Likewise, this figure details the number of articles excluded at different moments of the peer-selection process. In all cases, articles that did not meet the inclusion criteria were excluded, and a total of 48 articles (10,20-66) were finally selected for the in-depth analysis of the full text. The results extracted from these 48 articles, with special attention to the nutrients for which significant associations were found with some of the diseases related to aging, can be consulted in the Appendix 1. A complete list of the nutrients related to aging is shown in table I. The scientific literature that supports the associations between each nutrient and the diseases is also shown in the table.

Associations were found between cardiovascular diseases and macronutrients, dietary fiber, sodium and vitamin D; between cancer and fatty acids; between diabetes and fatty acids, fiber and simple sugars; between osteopenia or osteoporosis and calcium and vitamin D; between sarcopenia (muscle mass loss) and proteins, calcium, and vitamin D; and cognitive impairment or cognitive decline was associated with fatty acids and folates.

All these nutrients for which associations were found were incorporated into the new index. Table II summarizes the design of HADI. The scoring for each nutrient is also presented in the

table assigning points, following the procedure described in the methods section. The total intake of liquids was added to the design due to its well-known relevance in dehydration.

To compare the five nutritional indexes, table III shows the results of all the indexes for both samples. Both samples obtain low scores in all the assessed indexes. In all cases, with the exception of AHEI, sample 2 obtained lower scores, but they were not statistically significant (values of $p > 0.05$).

The scores obtained for the modified MDS (which measures adherence to the Mediterranean diet) were 4.46/9 and 4.13/9 in samples 1 and 2, respectively. These results point to a higher degree of adherence to the Mediterranean diet of metropolitan participants compared to rural participants. This result was not statistically significant (p -value = 0.07).

The behavior of HADI is similar to that of the previously evaluated indexes, since the scores obtained were 6.24/14 and 6.10/14 in samples 1 and 2, respectively, also obtaining sample 2 the lowest score.

DISCUSSION

The index proposed in this study (HADI) measures the adequacy of nutrients and diet for a healthy aging, and also takes into account the adequacy of nutrient intake for this purpose.

According to the scores obtained in all the assessed indexes, participants of both samples poorly meet the nutritional requirements to achieve a healthy aging. For this reason, the results obtained with the HADI, especially designed for healthy aging, showed the same behavior as the general nutritional indexes, obtaining 46.1% and 43.6% in samples 1 and 2, respectively. When comparing this result with the rest of indexes for samples 1 and 2, the AHEI obtained 35% and 35.8%, respectively; the HDI, 27.9% and 27.1%, respectively; the DQI, 40.8% and 40.1%, respectively; and the dietary index MDSmod reached the highest result, with 49.5% and 45.9%, respectively. Sample 2 scored lower on all indexes. Comparing it with the scores obtained by sample 1, it would be indicating the existence of a diet farther from the optimal point in relation to the adequacy of the diet for healthy aging.

Those results do not differ substantially from other studies conducted outside and within Europe, where the AHEI scores presented are generally low. In a study carried out among 71,495 women and 41,029 men in the USA, the average AHEI values were 52.9% and 58.2%, respectively (67). The AHEI showed similar results in the United Kingdom after being applied

to a large sample of the population (68). In the United States and Canada, the DQI obtained 51.8% of the maximum score and the HDI did not reach 39% (69). However, other studies offer results in another direction, with scores for this same index which are much higher. In an extensive review developed by Fernandes et al. in 2015 (70), which included eleven international studies, the AHEI scores varied from 56.7% to 96.3%. In the Spanish study analyzed in this review, the AHEI was calculated to 29,478 people and the subset of older people obtained the highest scores (average of 85.7%), with significant differences with respect to the other age groups (71).

In relation to specific indexes to evaluate the Mediterranean diet, such as the MDSmod, adherence to the pattern is usually higher in Spain among women, the elderly and among the more physically active participants (72). It is possible to find studies in the literature reporting an inverse trend for other European countries with different dietary patterns such as Sweden (73).

It is recognized that nutritional indexes are useful and validated tools to assess the quality of the diet of populations (12,13,71). The differences in the scores presented in different publications indicate quite clearly that the scores obtained in the different dietary indexes depend on the dietary patterns of the geographical area where they have been applied and other factors related to the fulfilment of a healthy life, some of which have been analyzed in this study.

Concerning the results shown in terms of demographic variables, our results are coincident with previous studies. The direct relationship between the best socioeconomic status in metropolitan areas and diet has been described in the literature as a general trend in developed countries (74).

Our review has identified nutrients directly involved in diseases related to aging. As far as the authors of this publication are aware, this complete collection of nutrients, which includes their attributes in healthy aging, has not been found in other studies nor has it been used in the design of validated nutritional indexes. This collection of nutrients adds useful evidence for the design of diets that allow healthy aging. The new index proposed in this study (HADI) is a tool of specific nutritional measurement in populations of advanced ages with risk of disability.

This study has some limitations. The data on exposure (nutritional data) and the effects analyzed in this study (diseases associated with aging) were collected at the same time and,

therefore, it is not possible to rule out inverse causality by not being able to determine a temporal sequence between causes and effects. However, significant associations have been found that give us clues to start up studies with epidemiological designs that allow establishing causal relationships. Therefore, further research is needed with other epidemiological designs (cohorts or case-control studies) to determine the causal relationships between the nutrients that are part of the diet and healthy aging.

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Table I. A. Bibliographic review: nutrients involved in healthy aging. Optimum intakes, findings related to aging and references

<i>Nutrient</i>	<i>Units</i>	<i>Women</i>	<i>Men</i>	<i>Findings related to aging</i>	<i>References</i>
Total hydric contribution	l/day	2.7	3.7	Prevents infections and the dehydration by deficits in renal function, thirst, and responses to osmotic and volume stimulation	16, 20, 21
Alcohol	g pure ethanol/day	10	20	Benefits of moderate consumption on cardiovascular disease (CVD)	15, 17, 22-23
Proteins	g/kg/day	0.8-1.2	0.8-1.2	Maintain lean body mass, promote recovery from illness, and maintain functionality	18-17, 24-25
Carbohydrates	% total kcal/day	> 50	> 50	Ensures energy enough that comes from food easily chewing and digestible Non-refined carbohydrates reduce CVD risk	15, 26-27
Simple carbohydrates	% total kcal/day	< 6	< 6	Greater consumption contributes to an increase in CVD incidence and worse cognition	15, 28-29
Total fiber	g/day	20-35	20-35	Beneficial effects of fiber on constipation and intestine function, blood lipid, glucose tolerance and kidney function	18, 28-30
Fatty acids	% total kcal/day	30-35	30-35	For maintaining adequate cognitive functioning, preventing or delaying the onset of dementia and ensuring the proper MUFA, PUFA, and fat-soluble vitamins intake	10, 15, 31
Saturate fatty acids	% total kcal/day	7-8	7-8	Greater intakes are related with CVD and neurodegeneration	10, 15, 31
Monounsaturated	% total	20	20	Decrease CVD and cognitive decline	10, 15, 31

fatty acids (MUFA)	kcal/day				
Polyunsaturated fatty acids (PUFA)	% total kcal/day	5	5	Prevent sarcopenia and decrease neurodegeneration and inflammation	15, 32-33
Trans fatty acids	% total kcal/day	< 1	< 1	They have adverse effects on cardiovascular health promoting inflammation, atherosclerosis and coronary heart disease	15, 34-35
Omega 6 fatty acids	% total kcal/day	3	3	Prevent sarcopenia and maintain cellular antioxidant status and stress response enzymes	15, 32-33
Omega 3 fatty acids	% total kcal/day	1-2	1-2	For preventing Alzheimer, dementia, sarcopenia and diabetes, as well as maintaining cellular antioxidant status and stress response enzymes	15, 32-33, 36
Cholesterol	mg/day	< 300	< 300	For preventing coronary heart disease and Alzheimer	15, 37-38
Calcium (Ca)	mg/day	1,300	1,200	Maintenance of healthy teeth and bones, cell signaling, coagulation, muscle contraction and neural transmission Prevents osteoporosis	16, 39-41
Iron (Fe)	mg/day	8-10	8-10	Necessary for proper function of both the innate and adaptive immune system Prevents anemia and is also involved in immune, cognitive and muscle function	16, 18, 40, 42
Copper (Cu)	mg/day	1.3-1.5	1.3-1.5	Essential cofactor for neurotransmitter synthesis and neuroprotection Contributes to protect the immune system and front to osteoporosis, CVD, alterations in cholesterol metabolism and Alzheimer	18, 43-44

CVD: cardiovascular diseases

Table I. B. Bibliographic review: nutrients involved in healthy aging. Optimum intakes, findings related to aging and references

<i>Nutrient</i>	<i>Units</i>	<i>Wome n</i>	<i>Men</i>	<i>Findings related to aging</i>	<i>References</i>
Iodine (I)	µg/day	90-150	90-150	Its deficiency is related to thyroid disease and its associated factors as swelling difficulty, dysphagia, dysphonia, or pain	16, 18, 45-46
Zinc (Zn)	mg/day	8-10	10-11	Normal growth and development, neurological function, wound healing and immune function Its deficiency is related to infections, diarrhea, dermatitis and reduced taste acuity	16, 44, 47
Sodium (Na)	mg/day	1,200- 2,300	1,200- 2,300	Greater intakes are related to CVD Lesser intakes are related to bone disease	18-19, 48-49
Phosphorus (P)	mg/day	700	700	It is associated with maintenance of the musculoskeletal system	15, 50-51
Selenium (Se)	µg/day	50-70	50-70	Its deficiency is related to poor muscle strength, immune function and cognitive decline	18, 52-53
Thiamine (B1)	mg/day	1.8	1.8	Necessary for proper energy production, nervous transmission, as well as the production of myelin for nerve conduction	18, 40, 55
Riboflavin (B2)	mg/day	1.5	1.5	Its deficiency is related to some types of cancer and CVD	15, 56
Pyridoxine (B6)	mg/day	1.5	1.7	Lower intakes are related to dementia, Alzheimer, vascular diseases and depression	15, 57-59
Folic acid (B9)	µg/day	300- 400	300-400	Positive association with cognitive function and negative association with dementia, Alzheimer, vascular diseases, anemia and depression	18-19, 57, 60

Cobalamin (B12)	µg/day	2.4-2.5	2.4-2.5	Positive association with cognitive function Lower intakes are related to dementia, Alzheimer, vascular diseases, anemia, decreased muscle strength and functional disability	15, 18, 60-61
Ascorbic acid (C)	mg/day	75-200	90-200	Protective for muscle loss Neutralizes the excess of free radicals, preventing cancer, autoimmune disorders, cataract, rheumatoid arthritis and cardiovascular and neurodegenerative diseases	15, 18, 62-63
Retinol (A)	µg/day	700	900	Neutralizes the excess of free radicals, preventing cancer, autoimmune disorders, cataract, rheumatoid arthritis and cardiovascular and neurodegenerative diseases	15, 40, 62
Calciferol (D)	µg/day	15	15	Prevents from skeletal muscle loss and improves regeneration Its deficiency is related to muscle weakness, CVD, neurocognitive dysfunction, common cancers and metabolic syndrome	58, 63-65
Tocopherol (E)	mg/day	15	15	Protective for muscle loss It also neutralizes the excess of free radicals, preventing cancer, autoimmune disorders, cataract, rheumatoid arthritis and cardiovascular and neurodegenerative diseases.	15, 62-63
Vitamin K	µg/day	90	120	Prevents osteoporosis by regulating the bone mineralization process It is also related to cognition maintenance	15, 40, 66

CVD: cardiovascular diseases.

Table II. Design of the Healthy Ageing Diet Index (HADI)

<i>Nutrient</i>	<i>Criteria (15-19)</i>	<i>Scoring</i>
Dietary fiber	20-35 g	1
Folates	300-1,000 µg	1
Calcium	1,000-1,300 µg	1
Sodium	1,200-2,800 mg	1
Vitamin D	5-10 µg	1
Total fat*	15-35% total daily energy consumed	1
Saturated fatty acids	< 10% total daily energy consumed	1
Monounsaturated fatty acids	> 15% total daily energy consumed	1
Essential fatty acids n-6 [†]	2-3% total daily energy consumed	1
Essential fatty acids n-3	1-2% total daily energy consumed	1
Cholesterol	< 300 mg	1
Total proteins*	0.8-1.5 g/kg	1
Simple sugars*	< 10% total daily energy consumed	1
Liquids	> 1,500 ml	1
<i>Optimal score</i>		<i>14 points</i>

*1 g of fat = 9 kcal; each gram of protein equals 4 kcal; each gram of sugars equals 4 kcal.

[†]Measured as linolenic acid.

Table III. Summary of indexes results (12,13)

Index	Target population	Outcome measure	Score range	Average score (CI 95%)		t-test (p-value)
				% of maximum score (CI 95%)		
				Sample 1	Sample 2	
HADI	Mediterranean elderly	Social and health care services	0-14*	6.45 (6.09-6.82)	6.10 (5.70-6.51)	0.21
		Chronic diseases		46.1 (43.5-48.7)	43.6 (40.7-46.5)	
		Autonomy level/functional Limitations				
		Disability				
MDSmod	European elderly	Cardiovascular disease	0-9*	4.46 (4.21-4.71)	4.13 (3.87-4.39)	0.07
		Chronic diseases		49.6 (46.7-52.3)	45.9 (43.0-48.8)	
		Mortality				
AHEI	Adults	Chronic disease risk	0-90*	31.52 (30.37-32.68)	32.22 (30.94-33.49)	0.43
HDI	Adults and elderly	Biomarkers	0-9*	2.51 (2.37-2.64)	2.44 (2.28-2.59)	0.47
		Mortality		27.9 (26.3-29.3)	27.1 (25.3-28.8)	
DQI	Adults and elderly	Biomarkers	0-16 [†]	9.47 (9.26-9.67)	9.58 (9.26-9.90)	0.55
		Mortality		59.2 (57.9-60.4)	59.9 (57.9-61.9)	

*The higher the score the better the score is. [†] The higher the score the worse the score is.

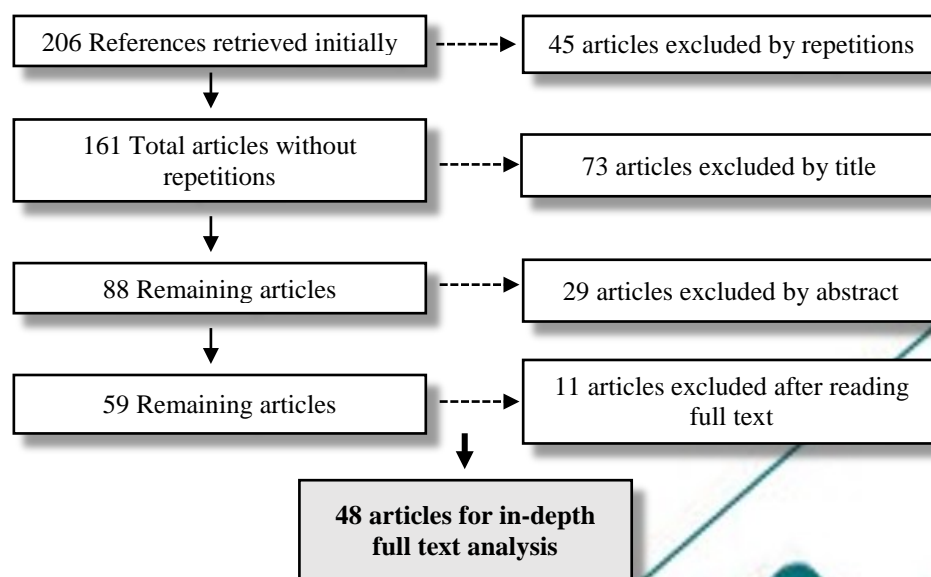


Fig. 1. Selection process of articles. Bibliographic review to identify nutrients involved in healthy aging.

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Appendix 1

Table A. Biographic review: main findings on the relationship of nutrients with age-related diseases

Article	Nutrient	Finding 1	Finding 2	Finding 3	Finding 4
20	Total hydric contribution	Prevention of urolithiasis and urinary tract infections	Prevention of constipation	Prevention of asthma and bronchopulmonary disorders	Prevention of cardiovascular diseases
21	Total hydric contribution	Supply impaired thirst perception	Supply reduced renal functions		
22	Alcohol (moderate)	Prevention of oxidative stress	Prevention of dementia	Psychosocial functioning maintenance	Lower dietary contributions
23	Alcohol (moderate)	Lower cardiovascular diseases death rate			
24	Proteins	Muscle function maintenance			
25	Proteins	Improves recovery from illness	Muscle mass maintenance	Muscle functionality maintenance	
26	Carbohydrates (high dietary glycaemic loads)	Higher cardiovascular diseases risk			
27	Carbohydrates (non-refined)	Lower cardiovascular diseases risk			
28	Simple carbohydrates	Higher Alzheimer's disease risk	Prevention of pre-dementia syndromes	Prevention of progression to overt dementia	
29	Simple carbohydrates	Higher cardiovascular diseases incidence			
30	Total fibre	Decrease in glucose absorption	Lipid lowering	Prevention of colon cancer and polyps	Prevention of constipation and diverticular disease
31	Fatty acids	Ensures the proper MUFA, PUFA and fat-soluble vitamins intake			
10	Fatty acids	Management of cognitive decline and dementia (MUFA, PUFA)	Decrease the cardiovascular diseases risk (MUFA)	Higher risk of neurodegeneration (SFA)	
32	Polyunsaturated fatty acids (long-chain)	Decrease neurodegeneration	Decrease inflammation		
33	Polyunsaturated fatty acids	Muscle mass maintenance	Antioxidant status maintenance		
34	Trans fatty acids	Higher cardiovascular diseases risk			

35

Trans fatty acids

Promote inflammation

Promote atherosclerosis

Promote coronary heart disease

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Table B. Biographic review: main findings on the relationship of nutrients with age-related diseases

Article	Nutrient	Finding 1	Finding 2	Finding 3	Finding 4
36	Omega 3 fatty acids	Promote type 2 diabetes			
37	Cholesterol	Prevention of coronary heart disease			
38	Cholesterol	Prevention of Alzheimer disease			
39	Calcium	Prevention of osteoporosis			
40	Calcium	Teeth and bones maintenance			
	Iron	Prevention of anaemia	Cognitive maintenance	Muscle function maintenance	
	Thiamine (B1)	Proper energy production	Proper myelin production for nerve conduction		
	Retinol (A)	Promote immunity	Night-time vision maintenance	Ocular health maintenance	Skin health maintenance
	Vitamin K	Prevention of osteoporosis by regulating the bone mineralization process			
41	Calcium	Prevention of osteoporosis	Cell signalling maintenance	Coagulation maintenance	Muscle contraction and neural transmission maintenance
42	Iron	Immunity maintenance			
43	Copper	Prevention of Alzheimer disease			
44	Copper	Neuroprotection from Alzheimer disease	Immunity maintenance	Prevention of osteoporosis	Prevention of cardiovascular diseases
	Zinc	Prevention of Alzheimer disease			
45	Iodine	Prevents thyroid diseases and its associated factors			
46	Iodine	Its deficiency is related with higher mortality risk			
47	Zinc	Immunity maintenance	Neurological function maintenance	Wound healing function maintenance	
48	Sodium	Increases the pulse pressure	Increase aortic rigidity		
49	Sodium	Low levels stimulate osteoclast genesis and bone resorptive activity			

Table C. Biographic review: main findings on the relationship of nutrients with age-related diseases

Article	Nutrient	Finding 1	Finding 2	Finding 3	Finding 4
50	Phosphorus	Osteoblast activity			
51	Phosphorus	Lower-extremity musculoskeletal maintenance			
52	Selenium	Low levels are associated with poor skeletal muscle strength			
53	Selenium	Antioxidant and anti-inflammatory effects to the production of thyroid hormone	Low levels are associated with poor immune function	Low levels are associated with cognitive decline	Higher levels have antiviral and reproduction effects
54	Selenium	Antioxidant role	Prevention of dementia	Low levels are related to Alzheimer disease	
55	Thiamine (B1)	Limited protection against cognitive decline and Alzheimer's disease			
56	Riboflavin (B2)	Lowers plasma homocysteine concentrations			
57	Pyridoxine (B6) Folic acid (B9)	Association through homocysteine levels to the risk of dementia	Association through homocysteine levels to Alzheimer's disease		
58	Pyridoxine (B6)	Positive correlation with local cortical folding			
59	Pyridoxine (B6)	Prevention of dementia and Alzheimer	Prevention of vascular diseases	Prevention of depression	
60	Folic acid (B9) Cobalamin (B12)	Prevention of cognitive impairment by inhibiting amyloid toxicity Positive association with cognitive function			
61	Cobalamin (B12)	Prevention of peripheral neuropathy	Muscle strength maintenance	Prevention of functional disability	
62	Ascorbic acid (C) Retinol (A) Tocopherol (E)	Neutralizes free radicals, preventing associated diseases			
63	Ascorbic acid (C) Cholecalciferol (D) Tocopherol (E)	Prevention of sarcopenia (muscle loss)			
64	Cholecalciferol (D)	Prevention of metabolic syndrome	Prevention of cardiovascular disease	Prevention of auto-immune diseases	Prevention of several types of cancer
65	Cholecalciferol (D)	Prevention of sarcopenia (muscle loss)	Muscle regeneration process maintenance		
66	Vitamin K	Cognition maintenance (consolidation of memory trace)			

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