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# Dietary Patterns and Healthy or Unhealthy Aging

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**Keywords**
Aging · Longevity · Healthy aging · Dietary pattern · Nutrition · Lifestyle · Diet · Ultra-processed food

**Abstract**
***Background:*** The aging process is complex, comprising various contributing factors influencing late-life conditions and eventual occurrence of chronic diseases that generate high financial and human costs. These factors include genetic proneness, lifestyle conducted throughout life, environmental conditions, as well as dietary aspects, among others, all together modulating precise pathways linked to aging, making longevity a multidimensional event. ***Summary:*** Compelling evidence support the concept that nutritional determinants have major impact on the risk of age-associated non-communicable diseases as well as mortality. Nutrition research has turned in recent years from considering isolated nutrients or foods to focusing on combinations of foods in dietary patterns in relation to their associations with health outcomes. This narrative review focuses attention on dietary patterns that may contribute to healthy or unhealthy aging and longevity with examples of traditional dietary patterns associated with healthy longevity and reviewing the association of healthy plant-based and unhealthy ultra-processed diets with frailty, a condition that may be considered a hallmark of unhealthy aging. ***Key Message:*** There is currently accumulated evidence confirming the key role that dietary patterns mainly of plant origin may exert in modifying the risk of age-associated chronic diseases and healthy longevity. These types of dietary models, unlike those in which the use of ultra-processed food is frequent, are associated with a reduced risk of frailty and, consequently, with healthy aging.



## Introduction

Population aging worldwide has a major impact on almost all aspects of society. A longer life expectancy is a triumph of humanity, which is expected to continue according to analyses of data from 195 countries showing that the estimated global life expectancy will increase by 4.4 years for men and women by 2040 to mean 74.3 years and 79.7 years, respectively [1]. The non-communicable diseases (NCDs) are chronic conditions associated with aging, which understandably are continuously increasing due to the aging of the world population. They comprise cardiovascular disease (CVD), diabetes, cancer, and neurodegenerative diseases, among others, which are responsible for about seventy percent of world mortality [2]. The increased morbidity derived from NCDs is not only associated with increased mortality but also with disability and worsening of quality of life. Therefore, efforts should aim in avoiding these diseases in order to promote healthy aging.

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One of the key factors contributing to this worrying scenario is the spread of unhealthy diets and lifestyles, which are established major risk factors for NCDs. Disability measured with disability-adjusted life years was largely ascribed to dietary risk factors in 2019: low dietary consumption of fruits and whole grains and high consumption of sodium are key factors increasing mortality and disability-adjusted life years worldwide [3]. Moreover, nutritional determinants associated with NCDs have increased substantially from 1990 to 2019.

Research dedicated to nutrition has considerably changed in the last decades. The former approach, also considered in dietary recommendations, was focused on nutrients or healthy foods. The shift in recent years is due to the notion that food and nutrient combinations conforming dietary patterns with their possible synergistic and antagonistic effects must be taken into account. This also may contribute to make messages and recommendations clearer to the lay public, who may have difficulty understanding abstract advice on nutrients and isolated foods rather than their combinations that are ultimately what they truly eat [4].

This narrative review focus attention on dietary patterns that may contribute to healthy and unhealthy aging with examples of traditional dietary patterns associated with healthy longevity and reviewing the association of plant-based and ultra-processed diets with frailty, a condition that may be considered a hallmark of unhealthy aging.

## Characteristics of a Healthy Dietary Pattern

The Dietary Guidelines for Americans (DGA) 2020–2025 [5] define a healthy dietary pattern as one that includes "nutrient-dense forms of foods and beverages across all food groups, in recommended amounts, and within calorie limits." These guidelines also describe how a healthy dietary pattern can impact health at any age, supporting well-being in the next life stages. Another key point raised by DGA 2020–2025 is that establishing a healthy dietary pattern early in life and sustaining it afterward may have a significant impact on minimizing the diet-associated chronic disease risk, in other words, promoting healthy aging. Contrarily, a dietary pattern full of different types of food and beverages that are not nutrient-dense may substantially contribute to disease expression later in life [5].

Therefore, it is recognized that a healthy dietary pattern delivers sufficient, but not excessive, amounts of macronutrients in order to cope with the energy and physiological needs, while also providing adequate hydration and enough micronutrients to the proper physiological body functions. Macronutrients, such as proteins, carbohydrates, and fats make accessible the energy needed for cellular processes in all the body organs. Essential micronutrients comprise vitamins and minerals, which are needed in small but adequate amounts for growth, metabolism, and general body-appropriate functions. Defining a healthy dietary pattern, even if not simple, is vital for delivering recommendations to the general public and in diverse specific clinical settings, and also for the development of strategies to improve the diet. It is fundamental to keep in mind that the recommended healthy dietary pattern may vary according to age, sex, disease status, and physical activity levels, as well as with the cultural context [6].

What are the components considered in a healthy dietary pattern? As mentioned, macronutrients are essential. First, carbohydrates are key energy sources mainly obtained with the consumption of grains, legumes, fruits, and vegetables. Whole grains should be preferred instead of refined grains lacking the bran and germ, which are lost during the milling process making them lower in fiber and micronutrients content. Meta-analyses of cohort studies have shown prospective associations of whole-grain consumption and lower risk of incident CVD, stroke, and cancer, together with lower total mortality risk and death as a result of cancer, CVD, diabetes, respiratory, and infectious diseases [6].

Second, the content of proteins in the diet providing energy and amino acids, comprising essential amino acids, is vital for the proper cellular functioning. Because the body cannot synthesize proteins, they must be consumed from animal (meat, fish, dairy, eggs) and/or vegetable (legumes, nuts, seeds, grains) sources. Proteins from animal sources contain all amino acids and are greatly bioavailable [7]. However, red and processed meat have been associated with an increased risk of mortality, CVD, and risk of incident breast, endometrial, colorectal, colon, rectal, lung, and hepatocellular cancer [8–10]. The mechanisms proposed for these harmful effects include the formation of n-nitroso compounds linked to the generation of colon cancer and also to the content of polycyclic aromatic hydrocarbons and heterocyclic aromatic amines, which are carcinogenic [11].

Dietary proteins are crucial to preserve muscle mass and function throughout life, particularly in later life when there is a tendency to develop sarcopenia (loss of muscle mass and function), a major risk factor for falls and fragility fractures [12]. Older adults are at high risk of malnutrition due to a number of concurrent factors, in particular inadequate protein intake [13] (Table 1); when protein cannot be obtained from the diet, the supplementation with oral amino acids can be helpful to sustain muscle strength [14].

**Table 1.** Age-related modifications and progressive cumulative risk of undernutrition in old age

| Changes with old age | Effects |
|---|---|
| Decreased sense of taste | Reduced appetite |
| Decreased sense of smell | Reduced appetite |
| Poor oral health | Difficulty chewing, chronic inflammation, poor quality diet |
| Loss of vision and hearing | Decreased ability to purchase and prepare food |
| Altered energy need | Diet lacking essential nutrients |
| Decreased physical activity | Progressive depletion of lean body mass and reduced appetite |
| Sarcopenia | Decreased functional ability, assistance needed with ADLs |
| Isolation | Decreased appetite |
| Financial | Limited access to food, poor quality diet |

ADL, activities of daily living.

Third, fats are a primary structural component of all cellular membranes and a crucial source of energy. A blend of different types of fatty acids (monounsaturated [MUFA], polyunsaturated [PUFA], saturated SFA], and transfats [TFA]) can be part of the diet. MUFA and PUFA dietary sources include vegetable oils, nuts, seeds, and fish. Saturated fats are mainly supplied by animal-derived foods and some vegetable oils. TFA are mainly processed products from the liquid-to-solid transformation of vegetable oils, although they can also be present in marginal amounts in some foods derived from animal sources. MUFA and PUFA have been associated prospectively with lower risk of mortality from CVD; conversely, TFA have been associated with various deleterious health effects, comprising CVD and mortality [15]. Omega-3 and omega-6 PUFA are essential for adequate growth and reproduction; they must be taken with diet because the body is not able to produce them. Some studies have shown cardio-protective effects of eicosapentaenoic acid and docosahexaenoic acid, together with prevention of cognitive decline, reduced inflammation, enhanced insulin sensitivity, and maintenance of muscle mass [16]. However, results are not homogeneous with other studies reporting neutral or even negative effects, specifically for cognitive performance [17]. Eicosapentaenoic acid and docosahexaenoic acid come mainly from fish consumption, while supplements are available for persons not meeting the recommended intake [18]. The main vegetable sources of omega-3 PUFA are nuts and seeds.

Other crucial components of dietary patterns promoting healthy aging are fresh vegetables and fruits, which are optimal sources of energy and fiber, enhance satiety, and provide favorable effects on bowel movement, blood lipid profile, and glycemic control [19]. This type of food is a key source of bioactive phytochemicals (e.g., polyphenols, carotenoids, and phytosterols), which may help explain the numerous health benefits associated with their consumption [20], linked to their antioxidant properties, actions on inflammatory mediators, fat metabolism, and nuclear transcription factors. As such, polyphenols, specifically flavonoids, have been reported to enhance insulin sensitivity that may help in the prevention of diabetes [21]. In addition, it has been reported that polyphenols affect the gut microbiota, stimulating the growth of favorable bacteria and generating additional bioactive compounds produced by these beneficial germs [21, 22]. High consumption of fruits and vegetables has been shown to be inversely associated with the risk of NCDs, including CVD, colorectal cancer, depression, hip fracture, stroke, and pancreatic diseases [23], as well as type 2 diabetes and gestational diabetes [24, 25].

Minerals and vitamins are essential for adequate growth, cellular integrity, and metabolism. Western diets, extensively spread worldwide, are characterized by a shift of whole food consumption to food choices that include plenty of refined, processed, and ultra-processed industrial foods, which have significantly contributed to a reduction in the supply of minerals and vitamins [26]. Inadequate intake of vitamins and minerals has been linked to cellular aging and the onset of NCDs in old age. Many of these components have recognized antioxidant actions (e.g., vitamins C, E, A, magnesium, selenium, copper, and zinc) that may contribute to reduce the risk and progression of NCDs linked to aging [27].

A dietary component frequently overlooked is the supply of liquids, despite the fact that water is the main component of the human body; it makes up most of the lean body mass and body weight. Water is not only a source of hydration but also of micronutrients,

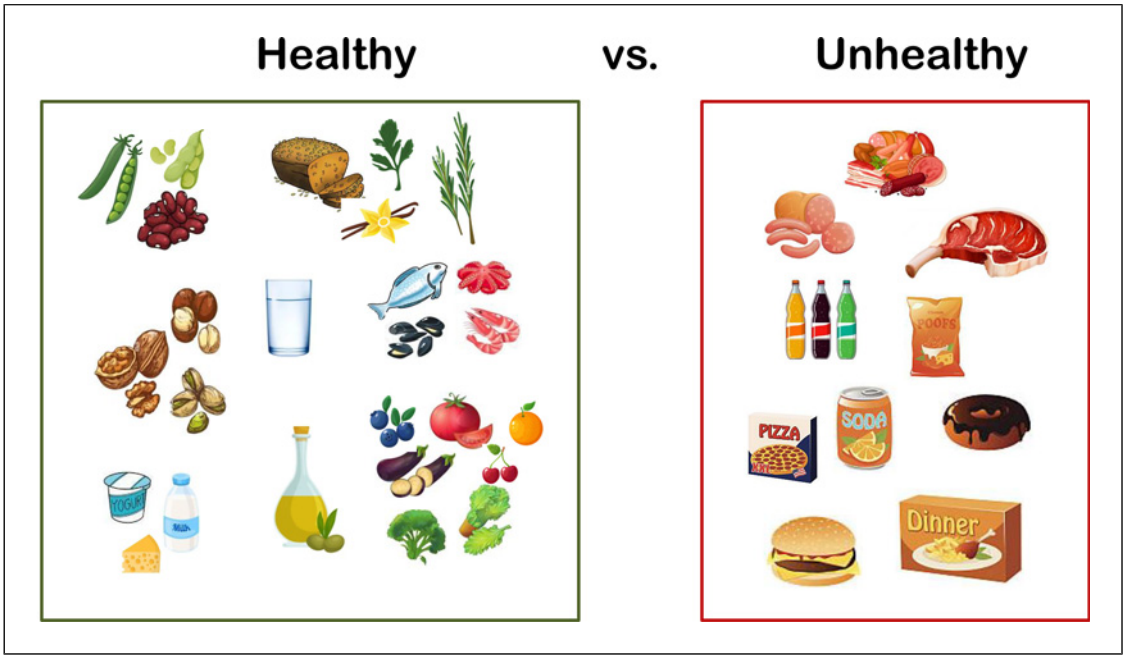


**Fig. 1.** Healthy and unhealthy dietary choices associated with reduced or increased risk of NCDs and longevity.

comprising electrolytes and trace elements [28]. Indeed, many other beverages contain bioactive components and energy but are often not considered in diet quality estimations. A recent analysis of data from the Seniors-ENRICA-1 cohort study showed that a healthy beverage score, indicative of the preference of healthy or unhealthy beverages, was strongly associated with incident frailty [29]. The healthy choices included the consumption of low-fat milk, tea/coffee, moderate intake of alcohol, and lower consumption of whole milk, fruit juices, and artificially and sugar-sweetened beverages. Therefore, based on current evidence of nutritional factors on health effects, a healthy dietary pattern can be defined as one that is rich in vegetables, fruits, whole grains, legumes, nuts, and vegetable oils, includes also low to moderate amount of fish, seafood, and poultry, low amounts of red meat, processed meat, added sugar, refined grains, and starchy vegetables, and that does not contain TFA [6] (Fig. 1).

## Examples of Dietary Patterns Associated with Lower Incidence of NCDs and Mortality

There are some traditional dietary patterns linked to cultural roots and comprising food sources produced in specific world geographic areas, which have been associated with healthy aging (Fig. 2). This is the case of Mediterranean diet, Japanese and Okinawan diet, vegetarian diet, as well as the more recently described Nordic diet. Other dietary patterns combining evidence-based healthy food choices focused on specific health outcomes have been developed. For example, the dietary approaches to stop hypertension (DASH) [30] and the Mediterranean Diet-DASH Intervention for Neurodegenerative Delay (MIND) that combines the former two healthy dietary patterns [31].

### Mediterranean Diet

This traditional dietary pattern consists of the consumption of foods that are fresh or minimally processed including the regular consumption of seasonal colorful vegetables and fruits daily; nuts and seeds in the traditional recipes or as snacks; various types of legumes consumed several times per week; unprocessed grains (pasta, bread, rice) consumed every day; cold pressed extravirgin olive oil consumed daily as the main source of dietary fat, for cooking and seasoning; use of herbs and spices for flavoring; consumption of fish in moderate amounts two to three times per week; daily consumption of dairy products, preferably low-fat milk and yogurt, as well as small portions of cheese occasionally; consumption of two to four eggs per week as sources of high-value proteins; sweets, cakes and dairy desserts consumed only occasionally few times per


**Fig. 2.** Main components of some traditional healthy dietary patterns associated with reduced risk of NCDs and longevity.

week; infrequent red and processed meat consumption in small portions (once to twice per month); drinking water as the main beverage; wine consumption in moderation (≤1 drink/day for women and 1–2 drinks/day for men) always with meals respecting beliefs of each community and former habits [32]. Mediterranean diet was designated as one of the healthiest dietary patterns in the 2015–2020 DGA [5]. Accumulating evidence has shown that a high adherence to the Mediterranean diet was associated with a reduced risk of total and cause-specific mortality, as well as a lower incidence of numerous age-associated chronic diseases comprising CVD, cognitive decline, dementia, depression, cancer (colorectal, breast, gastric, respiratory, bladder, liver, and head and neck cancer), type 2 diabetes, chronic obstructive respiratory disease, frailty, and fragility fractures [32]. For further detailed information, it is recommended to consult the review article by Guash-Ferre and Willett [33]. In summary, Mediterranean diet is considered a paradigm of a healthy dietary pattern with the largest evidence in the medical literature compared to other dietary models.

### Okinawan Diet

The Okinawa prefecture in Japan is home to the population with the greatest number of centenarians in the world. According to data from the Japan Ministry of

Health, Labor and Walfare, Okinawan women had a life expectancy of 87.02 years and men, 79.40 years, in 2013 [34]. Together with exceptional longevity, they also maintain an active life at a late age. About 80% of the calorie source in the Okinawan diet comes from plant-based foods comprising vegetables, fruits, whole grains, legumes (particularly soy), and small amounts of fish and lean meats [35]. People from Okinawa may represent a natural example of caloric restriction with optimal nutrition, which has been associated with longevity [36]. In fact, they follow the Confucian teaching of "*hara hachi bu*" [37], which is indeed a sort of caloric restriction: they learn to stop eating when they reach about 80% of total satiety. The incidence of colon, prostate, and breast cancer is about fifty percent lower among Okinawans compared to the rest of Japan [35]. They also have a reduced incidence of coronary heart disease, stroke, and other cerebrovascular diseases compared to the rest of Japan [35, 36, 38]. Okinawans have a very low prevalence of obesity and type 2 diabetes compared to populations from the USA or Europe [36].

### Japanese Diet

Japan is the country with the longest life expectancy in the world, the largest number of centenarians, and the fastest increase of aging in the world [39]. Japanese women had an increase in life expectancy of 3 months every year for 160 years in 2002 [40]. The Japanese diet is mainly based on small portions of traditional seasonal foods (vegetables, rice, fish, soy, green tea, and seaweeds) [37]. Rice is the main source of carbohydrates, accounting to 60–65% of total calories; about 20–25% of energy comes from fats, while proteins (mainly plant-based) account for 5–10% of energy. The Japanese diet has a lower content of fats versus the Mediterranean diet with an omega-6/omega-3 ratio of about 2–3 [41]. A higher adherence to the Japanese diet has been shown to be associated with reduced total and CVD-associated mortality and a lower incidence of cerebrovascular disease. The Japanese population included in the Seven Countries Study showed, together with the Mediterranean population, a reduced incident CVD and total mortality when compared with populations from the USA and Finland, results that have been confirmed in recent studies by Shirota et al. [42]. Recent studies have also shown an inverse association of a higher adherence to the Japanese dietary pattern with a lower risk of disability and incident Alzheimer's disease [43]. In summary, available evidence suggests that the traditional Japanese dietary pattern can be considered one of the determinants of the exceptional and healthy longevity observed in the Japanese population versus Western populations.

### Nordic Diet

This dietary pattern comprises foods consumed in five Nordic countries: Denmark, Norway, Finland, Sweden, and Iceland, where the typical dietary components include a high consumption of fish, root vegetables, cabbages, berries, apples, pears, whole grains, potatoes, low-fat dairy products, and rapeseed oil. Even if the Nordic diet has been studied only in recent times, the available literature on this dietary pattern is growing, showing significant associations of high adherence of Nordic diet with several NCDs and mortality. In particular, Nordic diet has been related with a reduction in CVD risk factors, improvement in blood lipid profiles, lower blood pressure in persons with cardiometabolic syndrome and central obesity, lower risk of type 2 diabetes, incident colorectal cancer, cognitive decline, ischemic stroke, and total mortality. For detailed information, it is recommended to consult the review by Renzella et al. [44] focusing on national and subnational Mediterranean diet and Nordic diet interventions and policies in the World Health Organization European Region in order to support decision-makers in shaping context-specific diet and nutrition policies.

Taken together, the Nordic dietary pattern has some evidence on protection against NCDs and promotion of healthy longevity. Nevertheless, further research is still needed to confirm the available results in all Nordic nations and in other populations.

### Vegetarian Diet

This type of diet is characterized by a total or partial exclusion of foods derived from animal sources. Vegetarian diets include abundant consumption of vegetables, fruits, grains, nuts, herbs, seeds, spices, mushrooms, and vegetable oils. There are variations of a vegetarian diet, such as vegan (exclusion of all animal products), raw vegan (using a temperature below 48°C for cooking), lacto-vegetarian, ovo-vegetarian, lacto-ovo vegetarian, and pesco-vegetarian [45].

Results from the Adventist Health Study 2 (AHS-2) showed that participants adhering more closely to all types of vegetarian diet had a lower risk of all-cause mortality. However, evaluating different types of vegetarianism only

pesco-vegetarians showed lower mortality, and the associations were more often significant in men compared to women [46]. Other studies have shown significant but smaller lower risk of CVD mortality, cerebrovascular disease, type 2 diabetes, and chronic kidney disease [47]. Taking into consideration 86 cross-sectional and 10 cohort studies, the vegetarian diet was associated with reduced body mass index, total and LDL cholesterol, and blood glucose levels. Prospectively, there was a reduced risk of coronary heart disease, mortality, and cancer, but no association with all-cause CVD and cancer mortality [48]. A meta-analysis including eight studies exhibited considerable heterogeneity, concluding that a vegetarian diet was associated with a modest CVD benefit but no clear lessening in total mortality [49]. Furthermore, it is not easy to identify whether the benefit of vegetarian diets may be attributable to the lack of meat consumption or to the abundant consumption of plant-derived foods. It is also crucial to take into consideration that a strict vegetarian diet may increase the risk of some nutritional deficits, such as vitamin B12, omega-3 PUFA, protein, calcium, vitamin D, iron, and zinc [47]. For further detailed information, it is recommended to consult the Proceedings of the Seventh International Congress on Vegetarian Nutrition [45].

### Association of Healthy Dietary Patterns and Chronic Diseases

As described in the examples of healthy dietary patterns mentioned above, there are numerous associations with these types of diet and various chronic diseases. A recently published study [50] aimed to compare the relative effectiveness of different healthy dietary patterns in reducing the risk of chronic diseases (i.e., CVD, cancer, diabetes) that are major causes of mortality in the USA. The study analyzed data from three large US cohorts (Nurses' Health Study [NHS], NHS II, and Health Professionals Follow-Up Study), comprising 205,852 participants with a median follow-up of 26 years. Even if, in general, adherence to one of the six healthy dietary patterns considered (Alternative Healthy Eating Index-2010 [AHEI-2010], Alternate Mediterranean Diet [AMED], DASH, Healthful Plant-Based Diet Index [hPDI], diabetes risk reduction diet [DDR], and World Cancer Research Fund/American Institute for Cancer Research [WCRF/AICR]) was associated with a decreased risk of major chronic diseases, there were some differences from each other in certain aspects. For example, the DASH diet was associated with a reduction in diabetes and CVD, while there was no association with total cancer. In the same study, while AHEI-2010 was associated with reduced risk of diabetes and CVD, a healthy diet, according to the WCRF, was not. Interestingly, participants who reported high adherence to two empirically constructed scores (reversed empirical dietary index for hyperinsulinemia [rEDIH] and reversed empirical dietary inflammation pattern [rEPID]) based on foods that are either positively or inversely associated with biomarkers of related biological pathways for chronic disease, i.e., hyperinsulinemia and chronic inflammation, and diabetes risk-reducing dietary patterns displayed a decreased risk for major chronic diseases when individually or as a composite outcome [50]. These two mechanisms being possible fundamental mediators of the association of healthy diets with prevalence or incidence of diseases, which are more or less crude endpoints, may help explain the sometimes different results when different definitions of a healthy dietary pattern are applied. Future studies are needed to verify these notable results in other populations and contexts.

### Association of Plant-Based Diets and Processed/Ultra-Processed Foods with Frailty

The aging process is so complex that it is difficult to identify a single appropriate marker to ascertain the eventual beneficial or harmful effects of a given nutritional pattern on longevity and/or on the incidence of NCDs. With the aim of exploring a possible marker of unhealthy aging, we reviewed the available studies that link plant-based dietary patterns and processed/ultra-processed foods with frailty, a condition that can be considered a hallmark of unhealthy aging. In fact, frailty is a geriatric syndrome whose frequency is increasing in parallel with population aging and is of great interest due to its dreadful consequences: increased disability, hospitalizations, falls and fractures, institutionalization, and mortality [51]. We acknowledge that some of the studies found in the searches were linked both to plant-based diets as well as with prevalent components of the Western diet, namely, processed/ultra-processed foods.

### Plant-Based Diets and Frailty

A literature search on the association of plant-based diets and frailty was conducted using two major databases, Embase and PubMed, from inception to June 8,

**Table 2.** Association of plant-based diets and frailty in cross-sectional studies

| Authors/country | Year | Participants | Exposure assessment method | Outcome assessment method | Main results |
|---|---|---|---|---|---|
| Bollwein et al. [52] Germany | 2013 | 192 community-dwelling older volunteers aged >75 years | Alternate MED score (proposed by Fung et al.) | Frailty phenotype (Fried et al.) | Frailty was identified in 15.1% of participants. The risk of being frail was significantly reduced in the highest quartile of the MED score (OR 0.26; 95% CI 0.07–0.98). |
| Ntanasi et al. [53] Greece, USA | 2018 | 1,740 participants aged ≥65 years from the Hellenic Longitudinal Investigation of Aging and Diet (HELIAD), | MDS (proposed by Panagiotakos et al.) | Frailty phenotype (Fried et al.), FI (Rockwood et al.), and Tilburg Frailty Identification | Frailty was identified in 4%, 18.7%, and 25.4% of participants according to the Fried et al. definition, the Frailty Index, and the Tilburg Frailty Indicator, respectively. Each additional unit in the MDS was associated with a 5%, 4%, and 7% decrease in the odds for frailty according to the three frailty definitions, respectively. |
| Lo et al. [54] Taiwan | 2017 | 923 noninstitutionalized participants aged ≥65 years enrolled in the Nutrition and Health Survey in Taiwan | Reduced Rank Regression was used to find a dietary pattern that explained maximal degree of variation of the frailty scores | Modified Fried criteria | Using nutritional survey datasets collected consecutively over 3 years from the beginning of 2014 to the end of 2016, a dietary pattern that is inversely associated with frailty in a dose-response manner was identified, validated, and confirmed. The derived dietary pattern was characterized with a high consumption of fruit, nuts and seeds, tea, vegetables, whole grains, shellfish, milk, and fish. |
| Ward et al. [55] USA | 2020 | 9,861 initially healthy US men, aged ≥60 years from the Physicians' Health Study | aHEI, MDS, and DASH | Cumulative deficit FI using 33 variables | The FI identified 38% of physicians as non-frail, 44% as pre-frail, and 18% as frail. Participants in the highest aHEI quintile had lower odds of frailty and pre-frailty compared with non-frailty (OR = .47; 95% CI = .39-.58 frailty; OR = .75; CI = .65-.87 for pre-frailty). Similar relationships were observed for DASH and MDS quintiles with frailty and pre-frailty. Restricted cubic splines showed an inverse dose-response relationship of diet quality scores with odds of frailty and pre-frailty. |
| Lo Buglio et al. [56] Italy | 2019 | 194 acute hospitalized patients ≥65 years | IMI (Agnoli et al.) | Frailty phenotype (Fried et al.) | Frailty was identified in 29.2% of third IMI tertile and in 100% of first IMI tertile. Multivariate analysis showed that a scarce adherence to IMI was an independent predictor of frailty status (OR: 7.792, p = 0.029). |

**Table 2** (continued)

| Authors/country | Year | Participants | Exposure assessment method | Outcome assessment method | Main results |
|---|---|---|---|---|---|
| Jayanama et al. [57] Canada | 2021 | 15,249 participants aged ≥20 years from the 2007–2012 NHANES | NI, E-DII™, HEI-2015, MDS, and DASH | 36-item FI (Rockwood et al.) | After adjusting for age, sex, race, educational level, marital and employment status, smoking, BMI, and study cohort, higher NI and E-DII scores and lower HEI-2015, MDS, and DASH scores were individually significantly associated with frailty. |
| Lim et al. [58] Taiwan | 2021 | 154 retirement home residents or community dwellers ≥65 years participating in congregate meal services | T-HEI, DASH, and MDS | Frailty phenotype (Fried et al.) | Linear regression model adjusted for age, gender, and functional ability showed that T-HEI was inversely associated with frailty status, but additional adjustment for nutritional status attenuated the association. A similar relationship was observed for DASH but not MDS. However, the distribution of whole grains component in both DASH and MDS was significantly higher in non-frail than prefrail and frail individuals. |
| Panagiotakis et al. [59] Greece | 2022 | 186 participants aged 60-89 years from a community-based study in Crete | MDS | FRAIL Questionnaire Screening Tool. | Multivariate analyses revealed a significant independent association of adherence to Mediterranean diet and frailty after adjusting for age, widowhood, social interactions/month, GDS score, polypharmacy, MMSE, waist circumference, and IL-6. |
| Wang et al. [60] China | 2021 | 780 participants aged 20–74 years from the Shanghai Suburban Adult Cohort and Biobank (SSACB) survey | CHEI, DASH, and MDS | Frailty phenotype (Fried et al.) | The prevalence of pre-frailty and frailty were 47.69% and 3.85%, respectively. Participants with a higher DASH score had lower frailty prevalence in the sex- and age-adjusted models. The association slightly strengthened in the multivariate adjusted model excluding participants with chronic diseases. High "protein-rich" dietary pattern scores were negatively associated with frailty prevalence in the multivariate adjusted model (OR = 0.82 (95% CI: 0.69–0.98). |

**Table 2** (continued)

| Authors/country | Year | Participants | Exposure assessment method | Outcome assessment method | Main results |
|---|---|---|---|---|---|
| Yaghi et al. [61] Lebanon, France | 2021 | 352 community-dwelling participants aged ≥60 years | Identification of dietary patterns via the K-mean cluster analysis method | FRAIL scale | A Westernized-type dietary pattern (WDP), a high intake/ Mediterranean-type dietary pattern (HI-MEDDP), and a moderate intake/ Mediterranean-type dietary pattern (MOD-MEDDP) were identified. In comparison to MOD-MEDDP, and after adjusting for covariates, adopting a WDP was strongly associated with a higher frailty prevalence in men (OR = 6.63, 95% (CI) (1.82–24.21) and in women (OR = 11.54, 95% (CI) (2.02–65.85). |
| Daou et al. [62] Lebanon, Qatar, United Arab Emirates, USA | 2022 | 112 community-dwelling older adults aged ≥65 years | LMD (Naja et al.) | Frailty phenotype (Fried et al.) | 14.3% participants were identified as frail. No significant association was found between LMD adherence and frailty in fully adjusted models. With a modified frailty index where house chores were not considered as part of leisure activities of the physical activity criterion, a higher LMD adherence was associated with significantly decreased frailty prevalence. |
| Ergul et al. [63] Turkey | 2022 | 200 hospitalized patients over 60 years old | EDI scoring (Kourlaba et al.) | FRAIL scale | According to the EDI scoring, the rate of unhealthy diets among study population was 91.5% and 56% of the patients were frail. EDI score was significantly related to frailty status and malnutrition. In a regression analysis the EDI score was an independent parameter for frailty (OR=0.826; %95 CI: 0.713–0.959; $p = 0.012$). |

aHEI, Alternative Healthy Eating Index; BMI, body mass index; CHEI, Chinese Healthy Eating Index; CI, confidence interval; DASH, Dietary Approaches to Stop Hypertension; E-DII™, energy-density Dietary Inflammatory Index; EDI, Elderly Dietary Index; FI, frailty index; GDS, Geriatric Depression Scale; HEI-2015, Healthy Eating Index-2015; IMI, Italian Mediterranean Index; LMD, Lebanese Mediterranean diet; MDS, Mediterranean diet score; Mini Mental State Examination; NHANES, National Health and Nutrition Examination Survey; NI, Nutrition Index; OR, odds ratio; T-HEI, Taiwanese Healthy Index.

2023. The search was based on the concepts of plant-based diets (vegetarianism, veganism, lacto-ovo-vegetarianism, Mediterranean, DASH diet). We considered observational studies without making exclusions by age, sex, or by the different definitions of plant-based diet or frailty criteria. Study selection and extraction were managed using Rayyan online software by two independent authors. From the 313 studies initially identified, 101 duplicate records were excluded and a total of 212 remaining records were screened at title/abstract level.

**Table 3.** Association of plant-based diets and frailty in observational prospective longitudinal studies

| Authors/country | Year | Participants | Exposure assessment method | Outcome assessment method | Follow-up | Main results |
|---|---|---|---|---|---|---|
| Talegawkar et al. [64] Italy, USA | 2012 | 690 community-living persons aged ≥65 years from the InCHIANTI study | MDS | Frailty phenotype (Fried et al.) | 6 years | Higher adherence to Mediterranean-style (MDS score ≥6) diet was associated with lower odds of developing frailty [OR = 0.30 (95% CI: 0.14, 0.66)] compared with those with lower adherence (MDS score ≤3). |
| León-Muñoz et al. [65] Spain | 2014 | 1,815 community-dwelling individuals aged ≥60 years | MEDAS and MDS | Frailty phenotype (Fried et al.) | 3.5 years | Compared with individuals in the lowest tertile of the MEDAS score, the OR (95% CI) of frailty was 0.85 (0.54, 1.36) in those in the second tertile, and 0.65 (0.40, 1.04; P for trend=0.07) in the third tertile. Corresponding figures for the MDS were 0.59 (0.37, 0.95) and 0.48 (0.30, 0.77; P for trend =0.002). |
| León-Muñoz et al. [66] Spain | 2015 | 1,872 non-institutionalized participants aged ≥60 years from the Seniors-ENRICA cohort | "prudent" dietary pattern and "Westernized" dietary pattern identified by factor analysis | Frailty phenotype (Fried et al.) | 3.5 years | During follow-up, 96 cases of incident frailty were ascertained. The multivariate OR (95% CI) of frailty among those in 3rd tertile of adherence to the prudent dietary pattern was 0.40 (0.2–0.81) versus the 1st tertile; P-trend = 0.009. The corresponding values for the Westernized pattern was 1.61 (0.85–3.03); P-trend = 0.14. A greater adherence to the Westernized pattern was associated with an increasing risk of slow walking speed and weight loss. |
| Chan et al. [67] China | 2015 | 2,724 Chinese community-dwelling men and women aged ≥65 years | DQI-I and MDS | FRAIL scale | 4 years | Factor analysis identified 3 a posteriori dietary patterns, namely "vegetables-fruits," "snacks-drinks-milk products," and "meat-fish." Every 10-unit increase in DQI-I was associated with 41% reduced risk of frailty in the sex- and age-adjusted model. The association attenuated in the multivariate adjusted model (OR 0.69 (95% CI: 0.47, 1.02), p = 0.056). No association between other dietary patterns and incident frailty was observed. |
| Rahi et al. [68] France | 2018 | 560 initially non-frail participants of the Three-City-Bordeaux study | MDS | Frailty phenotype (Fried et al.) | 2 years | Over the 2-year follow-up 14% of participants became frail. Older adults with the highest MDS (score 6-9) had a significantly 68% frailty risk reduction (95% CI: 28, 86%, p < 0.006) compared to those in the lowest MDS (score 0-3). |
| Veronese et al. [69] Italy, UK | 2018 | 4,421 participants at higher risk or having knee osteoarthritis from the OAI | MDS (proposed by Panagiotakos et al.) | SOF index | 8 years | During the 8 years follow-up participants with the highest aMED scores had a significant reduced incident frailty (HR=0.71; 95% CIs: 0.50, 0.99, p= 0.047) versus those in a lower category. with higher risk of frailty. |

**Table 3** (continued)

| Authors/country | Year | Participants | Exposure assessment method | Outcome assessment method | Follow-up | Main results |
|---|---|---|---|---|---|---|
| Lopez-Garcia et al. [70] Spain, USA | 2018 | 8,970 women aged ≥60 y with type 2 diabetes from the Nurses' Health Study | aMED score (proposed by Fung et al.) | FRAIL scale | 22 years | During follow-up 569 incident cases of frailty were identified. After adjustment for lifestyle factors and medication use, the HR (95% CI) of frailty was 1 for the lowest quartile of the aMED score, 0.88 (0.71, 1.10) for the second quartile, 0.69 (0.53, 0.88) for the third quartile, and 0.54 (0.42, 0.71) for the highest quartile (P-trend < 0.001). A 2-point (~1 SD) increase in the aMED score was associated with a 28% (95% CI: 19%, 36%) reduced risk of frailty. |
| Parsons et al. [71] UK | 2019 | 945 men from the British Regional Heart Study aged 70–92 years with no prevalent frailty | HDI based on WHO dietary guidelines and EDI based on a Mediterranean-style dietary intake | Frailty phenotype (Fried et al.) | 3 years | Men in the highest EDI category and those who followed a prudent diet were less likely to become frail [top versus bottom category OR (95% CI) 0.49 (0.30, 0.82) and 0.53 (0.30, 0.92) respectively, after adjustment for potential confounders including BMI and prevalent CVD. No significant association was seen for the HDI. By contrast those who had a high fat low fiber diet pattern were more likely to become frail [OR (95% CI) 2.54 (1.46, 4.40)]. |
| Ortola et al. [72] Spain | 2019 | 2,042 participants aged ≥60 years from the Seniors-ENRICA cohort | MEDAS, MDS, and AHEI-2010 | 52-item FI (Rockwood et al.) | 3 years | Compared with participants with a >1-point decrease in MEDAS or MDS, those with a >1-point increase showed lower FI from wave 0 to wave 2 (multivariate b: −1.49 [95% CI: −2.88 to 0.10], P-trend = .04 for MEDAS; and −2.20 [95% CI: −3.56 to −0.84], P-trend = .002 for MDS). Participants with a >5-point increase in AHEI-2010 showed lower FI from wave 0 to wave 1 (−1.15 [95% CI: −2.01 to −0.28], P-trend = .009) and from wave 0 to wave 2 (−1.21 [95% CI, −2.31 to −0.10], P-trend = .03) than those with a >5-point decrease. |
| Alaghehband et al. [73] Finland, UK | 2021 | 440 women aged 65–72 years from the OSTPRE-FPS | BSD and MDS | Frailty phenotype (Fried et al.) | 3 years | At 3-year follow-up, 46.8% were prefrail and 8.2% were frail. After adjusting for confounders, a tendency was found between BSD per SD-unit increase and lower likelihood of frailty (P = 0.057). MED per SD-unit increase was associated with lower likelihood of prefrailty (P = 0.009). |
| Struijk et al. [74] Spain, USA | 2020 | 71,941 women aged ≥60 y participating in the Nurses' Health Study | AMED, DASH, and AHEI-2010 | FRAIL scale | >22 years | During follow-up 11,564 incident cases of frailty were identified. After adjusting for potential confounders, the RRs (95% CIs) of frailty per 1-SD increase in the AMED, DASH, and AHEI-2010 scores were 0.87 (0.85, 0.90), 0.93 (0.91, 0.95), and 0.90 (0.88, 0.92), respectively. |

**Table 3** (continued)

| Authors/country | Year | Participants | Exposure assessment method | Outcome assessment method | Follow-up | Main results |
|---|---|---|---|---|---|---|
| Tanaka et al. [75] Italy, USA | 2021 | 485 community-living persons aged ≥65 years from the InCHIANTI study | MDS | FI (Rockwood et al.) | 10 years | High or medium MDS were associated with 0.03- and 0.013-unit lower FI scores over the follow-up period, compared to the low adherence group. In participants with a low FI at baseline, those with high or medium MDS had 0.004 and 0.005 unit/year slower progression of FI compared to the low adherence group. |
| Gängler et al. [76] Switzerland, France, USA | 2022 | 1,811 participants of DO-HEALTH trial without frailty at baseline aged ≥70 years | MDS (proposed by Panagiotakos et al.) | Frailty phenotype (Fried et al.) | 3 years | A five-point increase in the MDS over three years was associated with lower odds of becoming pre-frail [OR (95% CI) = 0.77 (0.68–0.88)] and frail [OR (95% CI) = 0.77 (0.64–0.92)]. Improved adherence to the Mediterranean diet over time was associated with significantly lower odds of becoming pre-frail or frail. |
| Maroto-Rodriguez et al. [77] Spain | 2022 | 1,880 participants aged ≥60 from the prospective Seniors-ENRICA-1 cohort | MEDLIFE index | Frailty phenotype (Fried et al.) | 3 years | After a 3.3-year follow-up, 136 incident frailty cases were ascertained. Compared with participants in the lowest tertile of the MEDLIFE score, the OR (95% CI) for frailty was 0.88 (0.58–1.34) for the second tertile, and 0.38 (0.21–0.69) for the third tertile (p-trend = .003). Blocks 1 and 3 of the MEDLIFE score were independently associated with lower frailty risk. Most items within these blocks showed a tendency to reduced frailty. |
| Millar et al. [78] USA | 2022 | 2,384 nonfrail adults from the Framingham Offspring Study | MSDPS | Frailty phenotype (Fried et al.) | 11 years | In adjusted models, a 1-unit higher MSDPS reduced the odds of frailty by 3% (OR, 0.97; 95% CI: 0.96–0.99). The associations among participants aged <60 years of age were stronger for each 1-unit higher MSDPS (OR, 0.93; 95% CI: 0.89–0.96) than those observed in older participants. |
| Ntanasi et al. [79] Greece, USA | 2022 | 1,075 Greek community-dwelling older adults from HELIAD | MDS (proposed by Panagiotakos et al.) | FI (Rockwood et al.), and Tilburg Frailty Identification | 3 years | 16.4% and 12.2% participants developed incident frailty, as measured with the FI and TFI, respectively. Each MDS unit was associated with a 5% (HR 0.95, 95% CI 0.91–0.99, p = 0.012) and 10% (HR 0.90, 95% CI 0.86–0.95, p ≤ 0.001) decrease in the risk of incident frailty when measured with the FI and TFI, respectively. Compared with participants reporting low adherence to the Mediterranean diet (lowest tertile), those with high adherence (highest tertile) had a 41% (HR 0.59, 95% CI 0.38–0.91, p = 0.017) and a 57% (HR 0.43, 95% CI 0.27–0.70, p ≤ 0.001) lower risk of incident frailty as measured with the FI and TFI, respectively. These results did not change after excluding from the analyses participants diagnosed with dementia at baseline or follow-up. |

**Table 3** (continued)

| Authors/country | Year | Participants | Exposure assessment method | Outcome assessment method | Follow-up | Main results |
|---|---|---|---|---|---|---|
| Sotos-Prieto et al. [80] Spain, USA | 2022 | 82,234 women aged ≥60 years from the Nurses' Health Study | hPDI and uPDI | FRAIL scale | >22 years | During follow-up, 12 910 incident cases of frailty were identified. In the multivariable analysis, the hPDI was inversely associated with a reduced risk of frailty (HR for the highest vs. lowest quintile: 0.77, 95% CI 0.72, 0.81; P trend <0.001). A 10-unit increment in the hPDI was associated with a relative 15% lower risk of frailty. Conversely, a direct association was found between the uPDI and risk of frailty (HR: 1.24 [1.17, 1.32], P trend <0.001). |
| Duan et al. [81] China | 2023 | 3,990 older adults from the Chinese Longitudinal Healthy Longevity Survey | PDI | Modified Frailty phenotype (Fried et al.) | 3 years | 557 cases of frailty were observed. After adjustment for covariates, the RR for frailty of a high PDI was 0.792 (95% CI: 0.644–0.973), versus a low PDI. Compared with respondents with a continually low PDI, the respondents with a continually high PDI had a significantly reduced risk of frailty (RR = 0.683, 95% CI: 0.514–0.908). |
| Maroto-Rodriguez et al. [82] Spain | 2023 | 1,880 participants aged ≥60 years from the Spanish Seniors ENRICA-1 cohort | uPDI and uPDI | Frailty phenotype (Fried et al.) | 3 years | After 3.3 years of follow-up, 136 incident frailty cases were ascertained. Comparing the highest versus the lowest tertile of adherence, the OR [95% CI] for frailty was 0.43 (0.25–0.74; p-trend = .003) for the hPDI, and 2.89 (1.73–4.84; p-trend < .001) for the uPDI. Higher consumption of healthy plant foods was inversely associated with frailty (0.39 [0.23–0.66; p-trend < 0.001]); higher consumption of unhealthy plant foods were associated with higher frailty risk (2.40 [1.23–4.71; p-trend = .01]). |

AHEI-2010, Alternative Healthy Eating Index-2010; aMED, alternate Mediterranean diet; BMI, body mass index; BSD, Baltic Sea Diet Score; CI, confidence interval; DASH, dietary approaches to stop hypertension; DQI-I, Diet Quality Index-International; DO-HEALTH, Vitamin D3-Omega3-home exercise-healthy aging and longevity trial; EDI, elderly dietary index; ENRICA, study on nutrition and cardiovascular risk in Spain; FI, frailty index; HDI, healthy diet indicator; HELIAD, Hellenic Longitudinal Investigation of Aging and Diet; hPDI, healthful plant-based diet index; HR, hazard ratio; InCHIANTI study: Invecchiare in Chianti study; MEDAS, Mediterranean Diet Adherence Screener; MDS, Mediterranean diet score; MEDLIFE, Mediterranean Lifestyle; MSDPS, Mediterranean-style dietary pattern score; OAI, Osteoarthritis Initiative; OR, odds ratio; OSTPRE-FPS, Osteoporosis Risk Factor and Prevention–Fracture Prevention Study; PDI, plant-based diet index; RR, risk ratio; RR, relative risk; SD, standard deviation; SOF, Study of Osteoporotic Fracture; uPDI, unhealthful plant-based diet index; WHO, World Health Organization.

After exclusion of non-human studies, abstracts, review articles, editorials, and perspective articles, 31 observational works (12 cross-sectional studies and 19 prospective studies) were finally identified.

### Cross-Sectional Studies

Table 2 summarizes the main characteristics and major findings of the 12 cross-sectional studies linking plant-based diets and frailty. As shown, for the evaluation of adherence to a plant-based diet, 9 of the 12 studies included Mediterranean diet scores, 4 evaluated Healthy Eating Index (HEI) with variations, 4 considered the DASH score, 2 used the Energy-Density Inflammatory Index, 1 used Nutrition Index, 1 used reduce rank regression analysis, and 1 performed cluster analysis. Similarly, for the evaluation of frailty, different methods were used including Frailty phenotype (Fried et al.), Frailty Index (Rockwood et al.), Tilburg Frailty Identification, and FRAIL scale.

**Table 4.** Association of processed/ultra-processed food diets and frailty in cross-sectional studies

| Author/ country | Year | Participants | Exposure assessment method | Outcome assessment method | Main results |
|---|---|---|---|---|---|
| Machón et al. [83] Spain | 2018 | 527 non-institutionalized functionally independent older people aged ≥70 years from Gipuzkoa (Spain) | MCA and cluster analysis identified dietary patterns and groups of individuals | TUG test | Frailty prevalence was 24.9%. A gradient of increasing frailty, poorer health status and worse dietary pattern, regarding recommendations, was observed among 3 cluster of participants. The third cluster gathered the oldest individuals, with more women (66.7%), lowest educational level, and frequently living alone. It had the highest prevalence of frailty (37.8%), the worst self-perceived health status, the highest prevalence of depressive symptoms, polypharmacy, fractures and falls, as well as more obesity, highest risk of malnutrition, and the lowest level of compliance with the SENC recommendation for vegetables, cereal, milk-dairy products, and fish-white meat-eggs-nuts-legumes intake, and the highest regarding red meat intake. |
| Jayanama et al. [57] Canada | 2021 | 15,249 participants aged ≥20 years from the 2007–2012 NHANES | NI, E-DII™, HEI-2015, MDS, and DASH | 36-item FI (Rockwood et al.) | After adjusting for age, sex, race, educational level, marital and employment status, smoking, BMI, and study cohort, higher NI and E-DII scores and lower HEI-2015, MDS, and DASH scores were individually significantly associated with frailty. |
| Hao et al. [84] China | 2022 | 2,329 participants from the NHANES 1999-2000 and 2001-2002 | UPFs were identified according to the NOVA classification | Modified Frailty phenotype (Fried et al.) | Pre-frailty or frailty was present in 45.6% of participants. In underweight-normal weight participants, every 100 kcal increase in energy of UPFs intake was associated with increased pre-frailty or frailty risk (OR: 1.08, 95% CI: 1.00-1.16, P = 0.045); every 10% increase in energy of UPFs intake was correlated with increase in pre-frailty or frailty risk (OR: 1.02, 95% CI: 1.00-1.03, P = 0.018). Similar results were found in overweight participants, with OR of 1.06 (95% CI: 1.01-1.10) and 1.01 (95% CI: 1.00-1.02), respectively (both P < 0.05). |

**Table 4** (continued)

| Author/ country | Year | Participants | Exposure assessment method | Outcome assessment method | Main results |
|---|---|---|---|---|---|
| Zupo et al. [85] Italy | 2023 | 2,185 older adults from the Salus in Apulia study | UPFs were identified according to the NOVA classification | Frailty phenotype (Fried et al.) | Eating more unprocessed or minimally processed foods was inversely related to nutritional frailty (co-presence of physical frailty and nutritional imbalance), even after adjustment (OR: 0.10, 95% CI 0.07–0.16). Moderate consumption of processed foods meant a nearly 50% increase in nutritional frailty probability (OR: 1.46, 95% CI 1.03–2.06), while the probability was double for the highest quintile against the lowest (OR: 3.22, 95% CI 2.27–4.58). |
| Yaghi et al. [61] Lebanon, France | 2021 | 352 community-dwelling participants aged ≥60 years | Identification of dietary patterns via the K-mean cluster analysis method | FRAIL scale | A Westernized-type dietary pattern (WDP), a high intake/ Mediterranean-type dietary pattern (HI-MEDDP), and a moderate intake/ Mediterranean-type dietary pattern (MOD-MEDDP) were identified. In comparison to MOD-MEDDP, and after adjusting for covariates, adopting a WDP was strongly associated with a higher frailty prevalence in men (OR = 6.63, 95% (CI) (1.82–24.21) and in women (OR = 11.54, 95% (CI) (2.02–65.85). |

BMI, body mass index; CI, confidence interval; DASH, Dietary Approaches to Stop Hypertension; EDI, Elderly Dietary Index; FI, Frailty Index; Healthy Eating Index-2015; MCA, Multiple correspondence analysis; MDS, Mediterranean diet score; NHANES, National Health and Nutrition Examination Survey; NI, Nutrition Index; OR, odds ratio; SENC, Spanish Society of Community Nutrition; TUG, Time-Up and Go; UPFs, ultra-processed foods.

Of the 12 cross-sectional studies identified, 10 showed a significant inverse association between greater adherence to a plant-based diet and a lower frequency of frailty. Only two studies were partially in the same direction. First, the study by Wang et al. [60] among participants from the Shanghai Suburban Adult Cohort and Biobank survey did not find any significant association between adherence to Mediterranean diet and frailty and between the Chinese Healthy Eating Index and frailty. Conversely, DASH score was inversely associated with frailty. Second, the study by Daou et al. [62] including community-dwelling older adults found no significant association between Lebanese Mediterranean diet (LMD) and frailty in fully adjusted models. With a modified frailty index where house chores were not considered as part of leisure activities of the physical activity criterion, a higher LMD adherence was associated with significantly decreased frailty prevalence.

### Longitudinal Prospective Studies

Table 3 summarizes the main characteristics and major findings of the 19 prospective studies linking plant-based diets and frailty. As for cross-sectional studies, various methods for assessing plant-based diets in the 19 longitudinal studies identified were used: 15 used Mediterranean diet adherence scores, 3 used plant-based adherence scores, 2 used the Alternative HEI-2010, and the following were only used in a single study: Diet Quality Index International, Healthy Diet Indicator,

**Table 5.** Association of processed/ultra-processed food diets and frailty in observational prospective longitudinal studies

| Authors/ country | Year | Participants | Exposure assessment method | Outcome assessment method | Follow-up | Main results |
|---|---|---|---|---|---|---|
| León-Muñoz et al. [66] Spain | 2015 | 1,872 non-institutionalized participants aged ≥60 years from the Seniors-ENRICA cohort | "Prudent" dietary pattern and "Westernized" dietary pattern identified by factor analysis | Frailty phenotype (Fried et al.) | 3.5 years | During follow-up, 96 cases of incident frailty were ascertained. The multivariate OR (95% CI) of frailty among those in 3rd tertile of adherence to the prudent dietary pattern was 0.40 (0.2–0.81) versus the 1st tertile; P-trend = 0.009. The corresponding values for the Westernized pattern was 1.61 (0.85–3.03); P-trend = 0.14. A greater adherence to the Westernized pattern was associated with an increasing risk of slow walking speed and weight loss. |
| Pilleron et al. [86] France | 2017 | 972 initially nonfrail nondemented participants aged ≥65 years from the Bordeaux sample of the Three-City Study | Five sex-specific dietary clusters | Frailty phenotype (Fried et al.) | 12 years | During follow-up, 299 participants became frail. In multivariate analyses, men in the "pasta" pattern and women in the "biscuits and snacking" pattern had a significantly higher risk of frailty compared with those in the "healthy" pattern (HR: 2.2; 95% CI: 1.1-4.4 and HR: 1.8; 95% CI: 1.2-2.8, respectively). |
| Laclaustra et al. [87] Spain | 2018 | 1,973 Spanish adults aged ≥60 years from the Seniors-ENRICA cohort | Tertiles of added sugar consumption | Frailty phenotype (Fried et al.) | 3 years | Compared with participants consuming <15 g/d added sugars (lowest tertile), those consuming ≥36 g/d (highest tertile) were more likely to develop frailty (OR: 2.27; 95% CI: 1.34, 3.90; P-trend=0.003). Association with frailty was strongest for sugars added during food production. Intake of sugars naturally appearing in foods was not associated with frailty. |
| Sandoval-Insausti et al. [88] Spain | 2020 | 1,822 Spanish adults aged ≥60 years from the Seniors-ENRICA cohort | UPFs were identified according to the NOVA classification | Frailty phenotype (Fried et al.) | 3.5 years | During follow-up, 132 cases of frailty were identified. The fully adjusted risks of frailty across increasing quartiles of the percentage of total energy intake from UPFs were the following: 0.04 (0.02–0.05), 0.05 (0.03–0.07), 0.09 (0.07–0.12), and 0.11 (0.08–0.14). Results were similar when food consumption was expressed as gram per day/body weight. |

**Table 5** (continued)

| Authors/ country | Year | Participants | Exposure assessment method | Outcome assessment method | Follow-up | Main results |
|---|---|---|---|---|---|---|
| Struijk et al. [89] Spain, USA | 2022 | 85,871 women aged ≥60 participants from the Nurses' Health Study | Consumption of total, unprocessed, and processed red meat | FRAIL scale | 22 years | During follow-up, 13,279 incident cases of frailty were identified. Women with a higher intake of red meat showed an increased risk of frailty after adjustment for lifestyle factors, medication use, and dietary factors. The RR (95% CI) for one serving/ day increment in consumption was 1.13 (1.08, 1.18) for total red meat, 1.08 (1.02, 1.15) for unprocessed red meat, and 1.26 (1.15, 1.39) for processed red meat. Replacing one serving/day of unprocessed red meat with other protein sources was associated with significantly lower risk of frailty; the risk reduction estimates were 22% for fish and 14% for nuts, while for replacement of processed red meat, the percentages were 33% for fish, 26% for nuts, 13% for legumes, and 16% for low-fat dairy. |
| Tanaka et al. [90] USA | 2022 | 1,024 BLSA participants aged ≥70 years | Carbohydrate Quality Indicators | FI (Rockwood et al.) | Mean 6.5 years (range 1–13.8 years) | In longitudinal analyses, there was a significant, positive association between higher tertiles of total carbohydrate, glycemic load, and non-whole grains and FI. Women in the highest tertile of the fiber-to-carbohydrate ratio showed a less steep increase in FI over time. |

BLSA, Baltimore Longitudinal Study of Aging; CI, confidence interval; HR: hazard ratio; FI, frailty index; OR, odds ratio; RR, relative risk; UPFs, ultra-processed foods.

Baltic Score Diet, DASH score, identification of prudent diet, and Elderly Dietary Index. For the evaluation of frailty, the same methods as for cross-sectional studies were used. The follow-up ranged from 2 to 22 years.

Out of 19 studies, 18 found a robustly significant inverse association between adherence to plant-based diets and incident frailty. Only one study by Chan et al. [67] was marginally significant. The authors found that every 10-unit increase in Diet Quality Index was associated with 41% reduced risk of frailty adjusted for sex and age, which significance was attenuated and marginally significant in multivariate adjusted models. There was no association between the other dietary patterns and incident frailty in this Chinese population of community-dwelling older adults.

In summary, practically all the studies, both cross-sectional and prospective, confirmed the association of greater adherence to a diet based mainly on foods of plant origin with a lower risk of becoming frail in old age. Indeed, plant-based dietary patterns, as in the examples shown above, are closest to the ideal of diets associated with healthy aging.

### Processed/Ultra-Processed Foods and Frailty

Healthy dietary patterns generally not only emphasize the high consumption of plant-based foods, such as fruit, vegetables, and whole grains, but also exclude the frequent consumption of unhealthy foods such as confectionary, meat, and processed/ultra-processed foods. In order to clarify whether there is evidence in the literature of the association between these unhealthy foods, we also performed a literature search on this specific aspect. In particular, we performed a similar literature search of the association between processed/ultra-processed foods and frailty using Embase and PubMed databases from inception to June 8, 2023. The search was based on the concepts of processed and ultra-processed foods/diets and frailty. From 863 studies initially identified in Embase and Pubmed, and after excluding 96 duplicate records, a total of 767 records were screened using Rayyan online software by two independent authors. After exclusion of non-human studies, abstracts, review articles, editorials, and perspective articles, 11 observational studies (5 cross-sectional studies and 6 prospective studies) were identified. As with the studies of plant-based diets identified, the methods used to assess the consumption of processed and ultra-processed foods were highly varied. Conversely, the frailty assessment used the same previous methods except for one study [83] that used the Time Up and Go test.

### Cross-Sectional Studies

Even if using heterogeneous methods, all five cross-sectional studies found that lower adherence to a healthy diet and/or increased consumption of processed and ultra-processed foods were associated with an increased presence of frailty (Table 4).

### Longitudinal Prospective Studies

All studies, despite heterogeneity in the assessment methods, found that a higher adherence to a Westernized diet and/or a higher consumption of processed meats, ultra-processed foods, added sugars, or refined carbohydrates were associated with a higher risk of developing frailty (Table 5).

## Conclusion

There is currently accumulated evidence confirming the key role that nutrition may exert in modifying the risk of NCDs and healthy longevity with examples of traditional dietary patterns, which support the beneficial effects of various food combinations mainly of plant origin. However, it is imperative to remember that today, most of the evidence available in nutrition research is based on observational studies, which have certain limitations; e.g., most of current knowledge is based on associations rather than effects. In addition, the observed associations cannot be explained following a reductionist's view searching for the molecular and cellular aspects, which may add to explain and thus substantiate the observations. However, recent results suggest that dietary patterns associated with low markers of insulinemia and inflammation had the largest risk reduction for incident major CVD, type 2 diabetes, and cancer as a composite and individually. These findings may inform on future dietary guidelines for chronic disease prevention.

It is clear that what is recommended for human health is a diet based mainly on plant products. In order to spread this type of message, it must be recognized that today there are some tools that may favor it, for example, digital systems that may help people be aware of their own food consumption and lifestyle; there is also growing interest in nutrition issues in medical schools to help people be aware of the outrageous human and financial costs that can come from making unhealthy food and lifestyle choices. Further efforts are still necessary to make healthy dietary and lifestyle choices available worldwide, rendering healthy eating broadly accessible and sustainable.


## Conflict of Interest Statement

The authors have no conflicts of interest to declare.

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## Author Contributions

Ligia J. Dominguez, Nicola Veronese, and Mario Barbagallo participated in the planning, literature search, and writing and critical revision of the paper.

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