

A Guide to Alzheimer's Prevention and Brain Function Enhancement

Edited by

Pengxu Wei

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Enhancement**

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Consensus on Nutritional Prevention and Intervention for Alzheimer's Disease and Related Dementias

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(Expert Consensus Working Group)

Abstract

Accumulating evidence indicates that a healthy lifestyle, including nutritious dietary patterns, can reduce the risk of Alzheimer's disease and other dementias. Building on recent research advances, this expert consensus offers food-based nutrition recommendations for the prevention and treatment of these conditions. Nutritional intervention should be an integral part of a healthy lifestyle, with a primary focus on healthy dietary patterns rather than specific nutrients. Implementing nutritional intervention requires providing a nutrition program—such as dietary guidelines, recommendations for healthy eating patterns, or nutritional prescriptions—to cognitively unimpaired individuals as well as those with mild cognitive impairment (MCI) or dementia. Daily energy requirements and other dietary reference intake (DRI) values should be tailored to the individual's age, gender, weight, nutritional status, physical activity level, and any existing health conditions. Nutrient intake

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should be balanced across a variety of foods. The application of healthy eating patterns must consider the specific needs related to Alzheimer's disease and dementia prevention. The effects of nutritional interventions should be monitored. Furthermore, prevention and intervention strategies for Alzheimer's disease and related dementias cannot rely solely on in-hospital care.

Keywords: Alzheimer's disease, dementia, cognitive impairment, nutrition, prevention, intervention, diet

Introduction

Cognitive health of elderly adults has become a significant global public health concern. During recent years, more than 9.9 million new cases of dementia emerge each year worldwide, i.e., around one new case per three seconds (Alzheimer's Disease International, 2015). It is estimated that the number of older adults suffering cognitive impairment or dementia will reach 78 million by 2030 and 139 million by 2050 (WHO, 2021) or even more (GBD 2019 Dementia Forecasting Collaborators, 2022).

Alzheimer's disease (AD) is the most common cause of dementia and accounts for about 60% to 80% of dementia cases (Alzheimer's Association, 2020). The disease is characterized by progressively worsening accumulation of amyloid- β ($A\beta$) plaques and neurofibrillary tangles formed by the microtubule-associated protein tau, with progressively worsening memory loss and other types of cognitive decline such as semantic comprehension errors, confusion, abnormal reasoning and decision-making processes (Han, Du, and Lim, 2021; Brito et al., 2023). Alzheimer's disease profoundly impacts the daily activities of patients, reduces their quality of life, and imposes a severe burden upon patients and their caregivers (Alzheimer's Disease International, 2015; Dolgin, 2016).

Alzheimer's disease is a continuum that ranges from a cognitively unimpaired stage to a severely demented status. The preclinical period of Alzheimer's disease may be a long period lasting several decades. Brain pathologies occur several decades before the onset of dementia (Jack Jr et al., 2018), and cognitive impairment may occur at a very early age. For instance, among people with a first-degree family history of Alzheimer's disease (first-degree relatives include an individual's parents, siblings, and offspring), cognitive functions such as verbal learning and memory may be slightly impaired at 18 years old, around 40 years before the typical onset of sporadic Alzheimer's disease (Talboom et al., 2019). When APOE ϵ 4 and a family history of Alzheimer's disease coexist, visuospatial and constructional skills may be impaired as early as the age of 11-16 years (Bloss et al., 2008).

Therefore, to prevent/postpone the progression of Alzheimer's disease pathology, potential risk factors should be identified and modified as early as possible. When Alzheimer's disease pathology progresses to the stage of mild cognitive impairment (MCI) or even early dementia, interventions may not successfully block the development of the pathological process (Mantovani et al., 2020).

Pre-dementia pathogenesis of Alzheimer's disease may be modified/mitigated by a healthy diet. Accumulating evidence supports that a healthy lifestyle including healthy dietary patterns, can reduce the risk of Alzheimer's disease and other dementias (Morris et al., 2003, 2006; Yu et al., 2020). Conversely, unhealthful diets, lack of physical activity, emotional stress, and other unhealthy lifestyle factors are associated with increased risks of Alzheimer's disease and other dementias. For instance, compared with controls, cognitive function in older adults (60-77 years old) can be improved by a 2-year multimodal intervention consisting of diet, exercise,

cognitive training, and vascular risk monitoring. Notably, the beneficial effects are regardless of several demographic and socioeconomic risk factors and apolipoprotein E4 types (Shannon et al., 2023).

Previous guidelines have not provided strong recommendations for nutritional interventions aimed at reducing the risk of Alzheimer's disease (AD). The WHO guideline on reducing the risk of cognitive decline and dementia strongly recommends a healthy, balanced diet for all adults (but not for reducing dementia risks). It also states that the Mediterranean-like diet may be recommended to adults with normal cognition and mild cognitive impairment to reduce the risk of cognitive decline and/or dementia. Additionally, it moderately advises against the use of Vitamin B and E, polyunsaturated fatty acids, and multi-complex supplements to reduce the risk of cognitive decline and/or dementia (WHO, 2019). The 2024 report from the Lancet standing Commission on dementia prevention, intervention, and care (Livingston et al., 2024) identified diet as a potential risk factor for dementia and noted that epidemiological studies often report inconsistent associations between diet and AD or dementia.

However, among the five cohort studies (Thomas et al., 2020; Agarwal et al., 2023; Glans et al., 2023; Gomes Gonçalves et al., 2023; Townsend et al., 2023), three systematic reviews/meta-analyses (Liu et al., 2020; Chen et al., 2023; Shannon et al., 2023), and a cross-sectional study (R Cardoso, Machado, and Steele, 2022) highlighted in the Lancet report (in the section Diet), most support a positive role of diet/dietary interventions in dementia prevention, except for the mentioned cross-sectional study and one cohort study. Additionally, a recent systematic review and meta-analysis (Rong et al., 2024) and two randomized clinical trials (Yeung et al., 2023; Ornish et al., 2024) consistently demonstrate the positive impact of

nutritional and dietary interventions on cognitive function in Alzheimer's disease patients. Therefore, based on the Grading of Recommendations Assessment, Development, and Evaluations (GRADE) approach (Guyatt et al., 2011), these findings strongly underscore the significant role of dietary interventions in the prevention and management of Alzheimer's disease.

Based on contemporary nutritional concepts and recent research advances, this expert consensus is developed by nationwide experts in China and provides food-based nutrition recommendations in the prevention and treatment of AD and other dementias.

Target Populations, Concepts, Principles, and Methods of Nutritional Prevention and Intervention

Target Populations

During the course of dementia development, cognitive performance exists on a continuum. Such cognitive continuum can be divided into three categories—cognitively unimpaired, mild cognitive impairment (MCI), and dementia, with dementia further subdivided into mild, moderate, and severe stages. Among cognitively unimpaired individuals, some may have subtle cognitive decline, e.g., subjective cognitive decline. For individuals in the Alzheimer's continuum, six numeric stages point to similar constructs: stage 1 describes an asymptomatic state, stage 2 corresponds to those with subtle (subjective/objective) cognitive decline, stage 3 corresponds to MCI, and mild, moderate, and severe dementia is identical to stages 4–6 (Jack Jr et al., 2018).

This consensus introduces principles, methods, and concepts of nutritional prevention and intervention for all adults and seniors (WHO, 2023) in the above categories/stages. However, compared to

patients with moderate or severe dementia, cognitively unimpaired individuals and those with MCI or mild dementia should be more likely to benefit from nutritional prevention and intervention for Alzheimer's disease and related dementias.

This expert consensus aims to provide practical nutritional prevention and intervention recommendations that can be implemented in the population to reduce the risk of Alzheimer's disease and related dementias.

Concepts of Nutritional Prevention and Intervention for Alzheimer's Disease and Related Dementias

The **Estimated Average Requirement (EAR)** is the average daily nutrient intake value to meet the requirements of 50% of healthy individuals within a group of the same life stage and gender (National Academies of Sciences and Medicine, 2023).

The **Recommended Dietary Allowance (RDA)** is the average daily level of intake sufficient to meet nutrient requirements of nearly all (97-98% or 97.5%) healthy individuals within a group of the same life stage and gender (Institute of Medicine (US) Committee to Review Dietary Reference Intakes for Vitamin D and Calcium, 2011; Chinese Nutrition Society, 2023).

The **Estimated Energy Requirement (EER)** is the average dietary energy intake that is predicted to maintain energy balance in a person according to a defined age, sex, weight, height, and level of physical activity (National Academies of Sciences and Medicine, 2023).

The **Adequate Intake (AI)** is the recommended average daily intake based on observed or experimentally determined approximations or

estimates of nutrient intake by a group (or groups) of individuals that are assumed to be adequate—used when an RDA cannot be determined (National Academies of Sciences and Medicine, 2023).

The **Tolerable Upper Intake Level (UL)** is the highest average daily nutrient intake that is likely to pose no risk of adverse health effects to almost all individuals in the general population; when intake increases above the UL, the potential risk of adverse effects may increase (National Academies of Sciences and Medicine, 2023).

The **Acceptable Macronutrient Distribution Range (AMDR)** is a range of usual intakes for a macronutrient that is associated with a reduced risk of chronic disease while providing adequate intakes of essential nutrients; an AMDR is expressed as a percentage of total energy intake (National Academies of Sciences and Medicine, 2023).

The **Chronic Disease Risk Reduction (CDRR)** intake value represents the relationship between a nutrient and the risk of chronic disease, e.g., reducing intake of sodium to 2300 mg/d or lower is associated with a decreased risk of hypertension and cardiovascular disease in adults (Chinese Nutrition Society, 2023; Heymsfield and Shapses, 2024).

Dietary reference intakes (DRIs) are a set of above reference values for nutrients.

—Values related to meeting nutritional requirements are: EAR, EER, RDA, and AI.

—The value for preventing excessive intakes is: UL.

—The values for reducing the risk of chronic disease are: CDRR and AMDR.

The physical activity level of Chinese adults is divided into three levels, i.e., low, moderate, and high intensities. In order to maintain a healthy weight, it is recommended that the physical activity level of an individual is maintained at 1.70 and above. People with low-intensity physical activity levels can achieve a physical activity level of 1.70 by performing 50~100 minutes of physical activity at moderate to high intensities every day (Chinese Nutrition Society, 2023).

Online calculators may be used to know DRI amounts for an individual (Heymsfield and Shapses, 2024). Note that DRI reference values may vary in different populations/countries (Chinese Nutrition Society, 2023). Also, note that each DRI reference value refers to the average daily nutrient intake to meet the nutrient requirements of most healthy individuals. In real life, deviation around this average value often exists over several days. For most healthy adults, nutrient amounts derived from day-to-day intake may vary substantially without ill effects observed in a short period (<https://www.nal.usda.gov/human-nutrition-and-food-safety/dri-calculator/>). It may be unrealistic to rigidly follow DRI reference values every day. However, frequent large deviations (e.g., from AMDR) can be detrimental to health (Chinese Nutrition Society, 2023).

Macronutrients are proteins, fats, and carbohydrates that serve as metabolic fuels and participate in many other vital functions.

Micronutrients are vitamins and minerals (Heymsfield and Shapses, 2024).

A **dietary pattern** is a combination of foods and beverages that constitutes an individual's complete dietary intake over time

(Dominguez and Barbagallo, 2018; US Department of Agriculture and US Department of Health and Human Services, 2020).

Food groups, e.g., vegetables, fruits, grains, protein foods, and oils, consist of subgroups. For instance, in the vegetable food group, there are dark-green vegetables; red and orange vegetables; beans, peas, lentils; starchy vegetables; and other vegetables (US Department of Agriculture and US Department of Health and Human Services, 2020).

Nutrient-dense foods and beverages provide vitamins, minerals, and other health-promoting components and have little added sugars, saturated fat, and sodium. Vegetables, fruits, whole grains, beans, peas, and lentils are nutrient-dense foods (US Department of Agriculture and US Department of Health and Human Services, 2020).

Ultra-processed foods are formulations of processed food substances (i.e., oils, fats, sugars, starch, and protein isolates) containing little or no whole foods (Livingston et al., 2024).

Most of the first DRI values were based on biological indicators related to inadequate intakes of nutrients. In recent decades, however, the focus has shifted from worries about nutritional deficiency diseases among population groups to concerns about the impact of diet on the risk of chronic diseases. Weight gain occurs when energy intake exceeds energy expenditure. Long-term energy intake imbalances are one type of dietary imbalance associated with the risk of chronic diseases (National Academies of Sciences and Medicine, 2023).

Principles and Methods of Nutritional Prevention and Intervention

Nutrition is Crucial for AD and Dementia Prevention/ Intervention

Based on the results of several systematic reviews, meta-analyses, and cohort studies with large sample sizes, high diet quality, compared with low diet quality, is associated with a decreased risk of dementia (Liu et al., 2020; Chen et al., 2023; Shannon et al., 2023; Townsend et al., 2023). High diet quality means adherence to specific dietary patterns, e.g., the Mediterranean diet, the Dietary Approaches to Stop Hypertension (DASH) diet, and the Mediterranean–DASH Intervention for Neurodegenerative Delay (MIND) diet (the Mediterranean diet plus specific healthy foods).

Additionally, these healthy dietary patterns are associated with decreased levels of amyloid β , phosphorylated tau, and global Alzheimer's disease pathology, reported in a cohort study with 581 older adults (Agarwal et al., 2023). A multicenter randomized controlled clinical trial, enrolled 51 early-stage AD patients, reported that a 20-week, plant-based diet and intensive lifestyle program can reverse cognitive decline and improve an AD-related plasma biomarker profile including plasma A β 42/40 ratio, phosphorylated Tau181, and glial fibrillary acidic protein (GFAP) compared with the usual-care control group (Ornish et al., 2024).

These findings indicate that healthy dietary patterns may protect cognitive function by delaying, blocking, and/or reversing AD-related pathological changes.

Nutritional Intervention should be an integral Part of a Healthy Lifestyle

Nutritional interventions should be adopted as an ingredient in a healthy lifestyle rather than a stand-alone approach. When other lifestyle differences were not taken into account, diet quality assessed during midlife was not significantly associated with subsequent risk for dementia during a period of the subsequent 9 years (Akbaraly et al., 2019). Conversely, a randomized controlled trial enrolling 2654 individuals found that a 2-year multidomain intervention, including diet, exercise, cognitive training, and vascular risk monitoring, could improve or maintain cognitive functioning in at-risk elderly people (Ngandu et al., 2015). Additionally, a cohort study (n=2449) found that a healthy lifestyle, including a Mediterranean-DASH dietary pattern, participating in cognitive activity in late life, moderate or high-level physical activity (≥ 150 min/week), no smoking, and mild or moderate alcohol intake (women 1-15 g/day; men 1-30 g/day), was associated with a longer life expectancy among individuals living a larger percentage of their remaining years without Alzheimer's dementia (Dhana et al., 2022). Another study showed that intensive lifestyle modification, including a healthy dietary pattern, can reverse cognitive decline in only 5 months for patients with MCI or mild dementia due to AD (Ornish et al., 2024).

A healthy lifestyle consisting of factors such as a healthy dietary pattern, sufficient and reasonable physical/cognitive activity, no smoking, limiting alcohol intake and frequent social contact can address modifiable risk factors for dementia. The healthy lifestyle should be adhered to early and kept throughout life (Livingston et al., 2024).

Focus Primarily on Healthy Dietary Patterns Rather Than Specific Nutrients

Foods are ingested in various combinations (i.e., a dietary pattern) but not in isolation. These ingested foods act synergistically to affect human health (US Department of Agriculture and US Department of Health and Human Services, 2020). Compared with single nutrients or components, a dietary pattern is more representative of how/what individuals eat and encompasses complex interactions between ingested nutrients (Liu et al., 2020).

Healthy dietary patterns share some similarities, such as a high intake of vegetables, fruits, whole grains, nuts and legumes, omega-3 polyunsaturated fatty acids, and low intake/avoidance of sugar-sweetened drinks and fruit juice, red and processed meat, trans fat, saturated fats, total dietary fat, and sodium (Akbaraly et al., 2019; US Department of Agriculture and US Department of Health and Human Services, 2020; Liu et al., 2020).

Examples of unhealthy foods are fried food, processed and red meat, pies, sweets, high-fat dairy products, and refined grains (Akbaraly et al., 2019).

Note that a healthy dietary pattern is not a rigid formulation. A dietary pattern consists of several food groups and subgroups in which there are different choices to meet the personal preferences of each individual (US Department of Agriculture and US Department of Health and Human Services, 2020).

Adhere to healthy dietary patterns early and throughout life

Ideally, a healthy dietary pattern, and other components of a healthy lifestyle, should be adhered to early and kept throughout life, i.e., the earlier, the better, and the longer, the better (US Department of

Agriculture and US Department of Health and Human Services, 2020; Livingston et al., 2024).

If a healthy dietary pattern is adopted in middle age or later, it may take a long period to show protective effects on cognitive function. A cohort study with a 24.8-year follow-up period found that diet quality scores (Higher scores representing a healthier diet) were significantly associated with lower risk of developing dementia at the 10th year of follow-up, whereas no significant association was detected in the first 9 years (Akbaraly et al., 2019).

Healthy Dietary Patterns for AD and Dementia Prevention/ Intervention

First, the calorie intake level should be determined based on an individual's gender, age, weight, height, physical activity level, and pregnancy or lactation status. A patient with specific health conditions probably needs modifications (Heymsfield and Shapses, 2024). Inadequate intakes of nutrients were major concerns when developing most of the first DRI values. However, currently, the role of long-term energy intake imbalances in the risk of chronic diseases, both energy intakes exceeding/lagging behind energy expenditure, should be considered. Too much energy intake results in overweight and obesity (National Academies of Sciences and Medicine, 2023), which shares overlapping neurodegenerative mechanisms with AD (Pugazhenthii, Qin, and Reddy, 2017). A study showed that those with higher calorie intake levels in middle age had lower cognitive function when they were over 75 years old (Fraser; Singh; Bennett, 1996).

For Chinese adults, the basal metabolic rate (BMR) and Estimated Energy Requirement (EER) can be calculated with the following formulas:

$$\text{BMR (kcal/d)} = 14.52 \text{ Weight (kg)} - 155.88(\text{male}=0, \text{female}=1) + 565.79$$

The above formula is suitable for adults aged 18-49 years. The calculated value $\times 95\%$ applies to those aged 50-64 years, $\times 92.5\%$ to those aged 65-74 years, and $\times 90\%$ to those aged ≥ 75 years.

$$\text{Estimated Energy Requirement (EER)} = \text{BMR} \times \text{PAL}$$

For a given individual, EER can be calculated based on the BMR per body weight (Kg) combined with the physical activity level (PAL). The physical activity levels of Chinese adults are divided into three levels, i.e., low, moderate, and high intensities. In order to maintain a healthy weight, it is recommended that the physical activity level of an individual is maintained at 1.70 and above. People with low-intensity physical activity levels can achieve a physical activity level of 1.70 by performing 50~100 minutes of physical activity at moderate to high intensities every day (Chinese Nutrition Society, 2023). Energy requirements are increased in pregnant and lactating women (WHO, 2023).

The metabolizable energy values for carbohydrates, fat, and protein (i.e., 4 kcal/g for carbohydrate and protein, and 9 kcal/g for fat) are not accurate but can provide estimates (Chinese Nutrition Society, 2023; Heymsfield and Shapses, 2024).

The core contents of healthy food patterns include vegetables, fruits (whole fruits but not fruit juice), grains (whole grains but not refined grains), protein foods (e.g., beans and nuts), and oils (e.g., plant oils) (Heymsfield and Shapses, 2024). Note that starchy vegetables, e.g., peas, potatoes, and corn, do not have the same health benefits as other vegetables and fruit juices do not have the same health benefits as whole fruits (Wang et al., 2021).

High intakes of foods containing high-quality carbohydrates, e.g., whole grains, fruits, vegetables, and pulses, can broadly improve health (WHO, 2023).

Based on the analysis including just under 135 million person-years of data from 185 studies and 4635 individuals from 58 clinical trials, a series of systematic reviews and meta-analyses found that higher intake of dietary fiber (25–29 g/d) was associated with the greatest reduced risk of all-cause mortality (among 25–29 g/d, 20–24 g/d, and 15–19 g/d). Note that dietary fiber intakes > 29 g/d (up to 35–40+ g/d) exhibit greater benefit. Similarly, higher whole grain intake (in the range of 0–360+ g/d) was associated with a greater reduction in risks of all-cause mortality, coronary heart disease, type 2 diabetes, and colorectal cancer. We, therefore, recommend a dietary fiber intake level of at least 25–29 g/d through regular consumption of rich sources of dietary fiber, e.g., vegetables, cereals, pulses (e.g. beans, peas, lentils), and whole fruit, and consumption of whole grains instead of refined grains (Reynolds et al., 2019). Dietary fiber also changes gut microbiota composition to correct gut microbiota dysbiosis that is associated with neurodegeneration (Gill et al., 2021).

The Acceptable Macronutrient Distribution Ranges for Chinese adults < 65 years old are 10 to 20% of calories for protein, 20 to 30% of calories for fat, and 50 to 65% of calories for carbohydrate; for Chinese adults ≥ 65 years are 15 to 20% of calories for protein, 20 to 30% of calories for fat, and 50 to 65% of calories for carbohydrate (Chinese Nutrition Society, 2023; WHO, 2023). These ranges are similar to those for American adults (10 to 35% of calories for protein, 20 to 35% of calories for fat, and 45 to 65% of calories for carbohydrate) (Agricultural Research Service, 2020; Heymsfield and Shapses, 2024).

People should meet macronutrient needs with nutrient-dense foods and beverages that can provide health-promoting components and have no or little added sugars and saturated fat. Examples of nutrient-dense foods and beverages are vegetables, fruits, whole grains, beans, peas, lentils, unsalted nuts, and seeds (US Department of Agriculture and US Department of Health and Human Services, 2020). Results from 2 large cohort studies and a meta-analysis showed that at least 3 servings of vegetables and 2 servings of fruits per day (80 g as a standard serving size) decreased the risk of total mortality. Additionally, higher intake of vegetables, but not fruits, was associated with additional risk reduction in neurodegenerative disease mortality (Wang et al., 2021). Another cohort study enrolled 960 individuals aged 58–99 years found that intake of green leafy vegetables was associated with slower cognitive decline; the highest group for green leafy vegetable intake (median of 1.3 servings/d) vs the lowest group (median of 0.09 servings/d) was the equivalent of about 11 years younger (Morris et al., 2018).

Note that ultra-processed food consumption increases the risk of AD and related dementias, proved by two large cohort studies (Gomes Gonçalves et al., 2023; Wang et al., 2023). Additionally, a cohort study of 493,888 participants found that a higher intake of processed meat (each additional 25 g/day) was associated with increased risks of incident all-cause dementia (Zhang et al., 2021).

Fat in food should be primarily unsaturated fatty acids, with no more than 10% of total energy intake from saturated fatty acids and no more than 1% of total energy intake from trans-fatty acids. Trans-fatty and saturated acids should be substituted with polyunsaturated fatty acids, monounsaturated fatty acids from plant sources, or carbohydrates from foods containing natural dietary fiber, e.g., whole grains, vegetables, fruits and pulses (Organization, 2023).

Polyunsaturated fatty acids (e.g., α -linolenic acid), monounsaturated fatty acids (e.g., olive oil), and nuts (e.g., walnuts) may slow cognitive decline and reduce dementia-related mortality. High saturated fat intake from milk products is associated with an increased risk of cognitive decline. Higher levels of intake of monounsaturated fatty acids from animal sources are associated with higher mortality due to neurodegeneration whereas an increase in those from plant sources is associated with lower mortality due to neurodegeneration (Sala-Vila et al., 2022; Liu et al., 2024; Tessier et al., 2024; Villos et al., 2024).

People should avoid intake of artificially sweetened soft drinks because these drinks are associated with an increased risk of ischemic stroke, dementia, and Alzheimer's disease (Pase et al., 2017).

A large cohort study found that alcohol intake was negatively associated with global brain volume, regional gray matter volumes, and white matter microstructure in middle-aged and older adults. Most of the detected negative associations are apparent in persons consuming an average of only one to two daily alcohol units (e.g., a pint or can of beer/lager/cider = two units, a 25ml single shot of spirits = one unit) (Daviet et al., 2022).

Multivitamin supplementation may help older adults improve cognitive function (Yeung et al., 2023).

Avoid eating food affected by environmental pollution, including pesticides and heavy metal residues, as toxicant exposure increases the risk of dementia (Genuis and Kelln, 2015; Domingo-Relloso et al., 2024; Tang, Shen, and Hong, 2024).

Implementation of Nutritional Prevention and Intervention

A growing body of evidence supports that nutritional and dietary interventions, e.g., a healthy diet have protective effects on cognitive function. Medical professionals in the field of cognitive impairment, neurodegenerative diseases, and geriatric diseases, including physicians, dietitians, nurses, etc., should pay more attention to nutrition and dietary measures in the prevention and intervention of cognitive disorders.

The implementation of the nutrition intervention requires the provision of a nutrition program (dietary guidelines, recommendations on healthy eating patterns, or nutrition prescription) to individuals, which consists of a group of food-based nutrition recommendations for the vast majority of individuals who are not hospitalized. According to the individual's age, gender, weight, nutritional status, physical activity level, existing health conditions, daily energy requirement (EER) and other DRI values are determined, and the intake of various nutrients is considered in a balanced manner. In addition, the application of healthy eating patterns needs to take into account the specificities of AD and dementia prevention.

The effects of nutritional interventions should be monitored. Changes in nutritional indicators, cognitive function, associated risk factors, and disease biomarkers can indicate whether an intervention is effective and help tailor the program. The indices that may be monitored include:

—General Nutritional Indicators: Body mass index (BMI), waist circumference, and body fatness (WHO, 2023).

—Intake levels of calories and macronutrients in foods, using reliable sources including Nutrition Facts labels.

—Risk factors for cognitive impairment and relevant chronic diseases, e.g., blood pressure, blood sugar, blood lipids, blood uric acid, and blood homocysteine.

—Cognitive function, including social cognition introduced in the Diagnostic and Statistical Manual of Mental Disorders, 5th Edition (DSM-5), e.g., poor theory of mind, reduced affective empathy, impaired social perception, or abnormal social behavior (American Psychiatric Association, 2013).

—AD-related biomarkers, e.g., blood biomarkers such as phosphorylated tau protein (p-tau217, p-tau181), glial fibrillary acidic protein, and neurofilament light chain (Jack Jr et al., 2024).

Nutritional prevention and intervention for Alzheimer's disease and related dementias cannot depend solely on in-hospital care. Only through health education can effective nutritional strategies be understood and adopted by the population, ultimately leading to a significant reduction in the prevalence of Alzheimer's disease.

Conflict of Interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

References

- Agarwal, P., Leurgans, S. E., Agrawal, S., Aggarwal, N. T., Cherian, L. J., James, B. D., Dhana, K., Barnes, L. L., Bennett, D. A., and Schneider, J. A. (2023). Association of Mediterranean-DASH Intervention for Neurodegenerative Delay and Mediterranean Diets With Alzheimer Disease Pathology. *Neurology* 100, e2259-2259e2268.
- Akbaraly, T. N., Singh-Manoux, A., Dugravot, A., Brunner, E. J., Kivimäki, M., and Sabia, S. (2019). Association of Midlife Diet With Subsequent Risk for Dementia. *JAMA* 321, 957-968.
- American Psychiatric Association, DSM-5 Task Force. (2013). *Diagnostic and statistical manual of mental disorders: DSM-5™* (5th ed.). American Psychiatric Publishing, Inc..
<https://doi.org/10.1176/appi.books.9780890425596>
- Alzheimer' Association. 2020 Alzheimer's disease facts and figures. *Alzheimers Dement.* 2020 ; 10.1002/alz.12068.
- Alzheimer's Disease International. World Alzheimer Report 2015-The Global Impact of Dementia. 2015. London. Alzheimer's Disease International.
- Bloss, C. S., Delis, D. C., Salmon, D. P., and Bondi, M. W. (2008). Decreased cognition in children with risk factors for Alzheimer's disease. *Biol. Psychiatry* 64, 904-906.
- Brito, D., Esteves, F., Rajado, A. T., Silva, N., ALFA score Consortium, Araújo, I., Bragança, J., Castelo-Branco, P., and Nóbrega, C. (2023). Assessing cognitive decline in the aging brain: lessons from rodent and human studies. *npj aging* 9, 23. doi: 10.1038/s41514-023-00120-6.
- Chen, H., Dhana, K., Huang, Y., Huang, L., Tao, Y., Liu, X., Melo van, Lent D., Zheng, Y., Ascherio, A., Willett, W., and Yuan, C. (2023). Association of the Mediterranean Dietary Approaches to Stop Hypertension Intervention for Neurodegenerative Delay (MIND) Diet With the Risk of Dementia. *JAMA Psychiatry* 80, 630-638.

- Chinese Nutrition Society. 2023. Dietary reference intakes for China (2023 edition). People's Medical Publishing House. 2023. Beijing.
- GBD 2019 Dementia Forecasting Collaborators. (2022). Estimation of the global prevalence of dementia in 2019 and forecasted prevalence in 2050: an analysis for the Global Burden of Disease Study 2019. *Lancet Public Health* 7, e105-105e125.
- Daviet, R., Aydogan, G., Jagannathan, K., Spilka, N., Koellinger, P. D., Kranzler, H. R., Nave, G., and Wetherill, R. R. (2022). Associations between alcohol consumption and gray and white matter volumes in the UK Biobank. *Nat Commun* 13, 1175. doi: 10.1038/s41467-022-28735-5.
- US Department of Agriculture and US Department of Health and Human Services. Dietary Guidelines for Americans, 2020–2025. 9th ed. Washington, DC: US Government Publishing Office; 2020. <http://dietaryguidelines.gov/>
- Dhana, K., Franco, O. H., Ritz, E. M., Ford, C. N., Desai, P., Krueger, K. R., Holland, T. M., Dhana, A., Liu, X., Aggarwal, N. T., Evans, D. A., and Rajan, K. B. (2022). Healthy lifestyle and life expectancy with and without Alzheimer's dementia: population based cohort study. *BMJ* 377, e068390. doi: 10.1136/bmj-2021-068390.
- Dolgin, E. (2016). How to defeat dementia. *Nature* 539, 156-158. doi: 10.1038/539156a.
- Domingo-Relloso, A., McGraw, K. E., Heckbert, S. R., Luchsinger, J. A., Schilling, K., Glabonjat, R. A., Martinez-Morata, I., Mayer, M., Liu, Y., Wood, A. C., Goldsmith, J., Hayden, K. M., Habes, M., Nasrallah, I. M., Bryan, R. N., Rashid, T., Post, W. S., Rotter, J. I., Palta, P., Valeri, L., Hughes, T. M., and Navas-Acien, A. (2024). Urinary Metal Levels, Cognitive Test Performance, and Dementia in the Multi-Ethnic Study of Atherosclerosis. *JAMA Netw Open* 7, e2448286. doi: 10.1001/jamanetworkopen.2024.48286.

- Dominguez, L. J., and Barbagallo, M. (2018). Nutritional prevention of cognitive decline and dementia. *Acta Biomed* 89, 276-290.
- Fraser, G. E., Singh, P. N., and Bennett, H. (1996). Variables associated with cognitive function in elderly California Seventh-day Adventists. *Am J Epidemiol* 143, 1181-1190.
- Genuis, S. J., and Kelln, K. L. (2015). Toxicant exposure and bioaccumulation: a common and potentially reversible cause of cognitive dysfunction and dementia. *Behav Neurol* 2015, 620143.
- Gill, S. K., Rossi, M., Bajka, B., and Whelan, K. (2021). Dietary fibre in gastrointestinal health and disease. *Nat Rev Gastroenterol Hepatol* 18, 101-116.
- Glans, I., Sonestedt, E., Nägga, K., Gustavsson, A. M., González-Padilla, E., Borne, Y., Stomrud, E., Melander, O., Nilsson, P. M., Palmqvist S., Hansson O. (2023). Association Between Dietary Habits in Midlife With Dementia Incidence Over a 20-Year Period. *Neurology* 100, e28-28e37. doi: 10.1212/WNL.0000000000201336.
- Gomes Gonçalves, N., Vidal Ferreira, N., Khandpur, N., Martinez Steele, E., Bertazzi Levy, R., Andrade Lotufo, P., Bensenor, I. M., Caramelli, P., Alvim de Matos, S. M., Marchioni, D. M., Suemoto, C. K. (2023). Association Between Consumption of Ultraprocessed Foods and Cognitive Decline. *JAMA Neurol* 80, 142-150.
- Guyatt, G., Oxman, A. D., Akl, E. A., Kunz, R., Vist, G., Brozek, J., Norris S., Falck-Ytter Y., Glasziou, P., DeBeer, H., Jaeschke, R., Rind, D., Meerpohl, J., Dahm, P., Schünemann, H. J. (2011). GRADE guidelines: 1. Introduction-GRADE evidence profiles and summary of findings tables. *J Clin Epidemiol* 64, 383-394.
- Han, J., Du, Z., and Lim, M. H. (2021). Mechanistic Insight into the Design of Chemical Tools to Control Multiple Pathogenic Features in Alzheimer's Disease. *Acc Chem Res* 54, 3930-3940.

Heymsfield, S. B., and Shapses, S. A. (2024). Guidance on Energy and Macronutrients across the Life Span. *N Engl J Med* 390, 1299-1310.

Institute of Medicine (US) Committee to Review Dietary Reference Intakes for Vitamin D and Calcium; Editors: A Catharine Ross, Christine L Taylor, Ann L Yaktine, and Heather B Del Valle. Dietary Reference Intakes for Calcium and Vitamin D. 2011. Washington (DC). National Academies Press (US).

Jack, C. R. Jr, Andrews, J. S., Beach, T. G., Buracchio, T., Dunn, B., Graf, A., Hansson, O., Ho, C., Jagust, W., McDade, E., Molinuevo, J. L., Okonkwo, O. C., Pani, L., Rafii, M. S., Scheltens, P., Siemers, E., Snyder, H. M., Sperling, R., Teunissen, C. E., and Carrillo, M. C. (2024). Revised criteria for diagnosis and staging of Alzheimer's disease: Alzheimer's Association Workgroup. *Alzheimers Dement* 20, 5143-5169.

Jack, C. R. Jr, Bennett, D. A., Blennow, K., Carrillo, M. C., Dunn, B., Haeberlein, S. B., Holtzman, D. M., Jagust, W., Jessen, F., Karlawish, J., Liu, E., Molinuevo, J. L., Montine, T., Phelps, C., Rankin, K. P., Rowe, C. C., Scheltens, P., Siemers, E., Snyder, H. M., and Sperling, R. (2018). NIA-AA Research Framework: Toward a biological definition of Alzheimer's disease. *Alzheimers Dement* 14, 535-562.

Liu, Y., Gu, X., Li, Y., Rimm, E. B., Willett, W. C., Stampfer, M. J., Hu, F. B., and Wang, D. D. (2024). Changes in fatty acid intake and subsequent risk of all-cause and cause-specific mortality in males and females: a prospective cohort study. *Am J Clin Nutr* 121,141-150.

Liu, Y. H., Gao, X., Na, M., Kris-Etherton, P. M., Mitchell, D. C., and Jensen, G. L. (2020). Dietary Pattern, Diet Quality, and Dementia: A Systematic Review and Meta-Analysis of Prospective Cohort Studies. *J Alzheimers Dis* 78, 151-168.

Livingston, G., Huntley, J., Liu, K. Y., Costafreda, S. G., Selbæk, G., Alladi, S., Ames, D., Banerjee, S., Burns, A., Brayne, C., Fox, N. C., Ferri, C. P., Gitlin, L. N., Howard, R., Kales, H. C., Kivimäki, M.,

- Larson, E. B., Nakasujja, N., Rockwood, K., Samus, Q., Shirai, K., Singh-Manoux, A., Schneider, L. S., Walsh, S., Yao, Y., Sommerlad, A., and Mukadam, N. (2024). Dementia prevention, intervention, and care: 2024 report of the Lancet standing Commission. *Lancet* 404, 572-628.
- Mantovani, E., Zucchella, C., Schena, F., Romanelli, M. G., Venturelli, M., and Tamburin, S. (2020). Towards a Redefinition of Cognitive Frailty. *J Alzheimers Dis* 76, 831-843.
- Morris, M. C., Evans, D. A., Bienias, J. L., Tangney, C. C., Bennett, D. A., Aggarwal, N., Schneider, J., and Wilson, R. S. (2003). Dietary fats and the risk of incident Alzheimer disease. *Arch Neurol* 60, 194-200.
- Morris, M. C., Evans, D. A., Tangney, C. C., Bienias, J. L., and Wilson, R. S. (2006). Associations of vegetable and fruit consumption with age-related cognitive change. *Neurology* 67, 1370-1376.
- Morris, M. C., Wang, Y., Barnes, L. L., Bennett, D. A., Dawson-Hughes, B., and Booth, S. L. (2018). Nutrients and bioactives in green leafy vegetables and cognitive decline: Prospective study. *Neurology* 90, e214-214e222.
- National Academies of Sciences, Engineering, and Medicine. 2023. *Dietary Reference Intakes for Energy*. Washington, DC: The National Academies Press. <https://doi.org/10.17226/26818>.
- Ngandu, T., Lehtisalo, J., Solomon, A., Levälahti, E., Ahtiluoto, S., Antikainen, R., Bäckman, L., Hänninen, T., Jula, A., Laatikainen, T., Lindström, J., Mangialasche, F., Paajanen, T., Pajala, S., Peltonen, M., Rauramaa, R., Stigsdotter-Neely, A., Strandberg, T., Tuomilehto, J., Soininen, H., and Kivipelto, M. (2015). A 2 year multidomain intervention of diet, exercise, cognitive training, and vascular risk monitoring versus control to prevent cognitive decline in at-risk elderly people (FINGER): a randomised controlled trial. *Lancet* 385, 2255-2263.