ISSN 2348-313X (Print)
International Journal of Life Sciences Research ISSN 2348-3148 (online)
Vol. 10, Issue 3, pp: (61-70), Month: July - September 2022, Available at: www.researchpublish.com

A Literature Review on Processed food and Alzheimer's risk

Paticha Kosonboon

Triam Udom Suksa School, Bangkok, Thailand

DOI: https://doi.org/10.5281/zenodo.7066486

Published Date: 10-September-2022

Abstract: **Approximately 44 million people worldwide have Alzheimer's disease (AD). Numerous claims have been made regarding the influence of diet on AD development. In particular, in today's world it is unavoidable to consume ultra-processed food as it provides people with a more convenient lifestyle. However, many previous researches have shown that ultra-processed food intake affects health outcomes, for example, metabolic diseases, cardiovascular problems, and also effects to cognitive function. Numerous studies on the effect of diet on Alzheimer's point to nutrition as a heavily influential factor in the development of dementia and Alzheimer's Disease (AD). This study systematically reviews these articles using the PubMed for articles published in English between 2017 and the end of July 2022 to understand the association between ultra-processed foods intakes and Alzheimer's disease. The results from this study suggest that, it should be considered as important to gain a better understanding of Alzheimer's disease pathogeneses. The association between Ultra-processed foods and Alzheimer's disease should be concerned. It is beneficial to discuss the evidences of recently established interventions considered to prevent or delay the prodromes of dementia and Alzheimer's disease and provide the prospective future directions in prevention and management of dementia and Alzheimer's disease. Diet is considered as important factors that help prevent or delay the development of Alzheimer's disease and other dementia-related diseases. Preventing or postponing the onset of Alzheimer's disease (AD) and delaying its progression would lead to an improvement of health status and quality of the older age life. This study also report the main findings that can guide further research.**

Keywords: **Ultra-processed foods, Western diet, Dementia, Alzheimer's disease, Processed foods.**

I. INTRODUCTION

In today's world, it is unavoidable to consume ultra-processed food as it provides people with a more convenient lifestyle. However, many researches have shown that ultra-processed food intake affects health outcomes, for example, metabolic diseases and cardiovascular problems. It also shows that there might be effects to cognitive function. Numerous studies on the effect of diet on Alzheimer's point to nutrition as a heavily influential factor in the development of dementia and Alzheimer's Disease (AD). This study systematically reviews these relevant articles to understand the association between ultra-processed food intakes and Alzheimer's disease, identify any issues and report the main findings that can guide further research.

II. OBJECTIVE

As numerous people in the society are suffering from Alzheimer's disease, it is very essential to learn about the risk of the disease and to gain a better understanding, especially the risk from what most people consume; Ultra-processed food. This study helps to analyze the current literature on Alzheimer's risk in relation to consuming processed foods.

III. METHOD OF STUDY

This was a small project to carry out a review of research in the area which was searched systematically for materials in PubMed for articles published in English since 2017 and up to the end of July 2022, using the main electronic sources expected to find relevant material. Furthermore, it was clear about the material to be selected to review. As is clear from

the search strategy, with the terms 'Processed foods', 'Ultra-processed foods' or 'Western Diet' appearing in the publication of the title, alongside 'Dementia' and/or 'Alzheimer'.

1. Ultra-processed foods

1.1 The meaning of Ultra-processed foods (UPF)

The original NOVA system of food classification was developed in 2010 by a Brazilian nutrition researcher, Carlos Monteiro, and his team, specifically to categorise the nature of industrial food processing. It was the first time that the concept of "ultra-processed food" was developed and coined (Croker, 2022). NOVA classifies all foods and food products into four groups according to the extent and purpose of the industrial processing they undergo. All physical, biological and chemical methods used during the food manufacturing process, including the use of additives, were considered (Monteiro et al, 2017). In a general term known, Ultra-processed food (UPF) or highly processed foods are foods that highly added sugar, salt and fats. They also contain food additives such as preservatives, color, flavours, but little. These foods go through multiple processes. Examples of these food are chocolate, candy, salty snacks, soft drinks, fries and frozen meals (McManus, 2020).

1.2 Nutrition and Inflammation

Ultra-processed foods mostly consist of sugar, fat, sodium, most Vitamin E and plant protein. Ultra-Processed foods can raise our blood sugar, they are also high in calories and unhealthy fats but low in fiber which benefits human's health. This can also lead to obesity. The World Health Organization (WHO) recommended limiting added sugar intake to no more than 10% of total energy intake, for greater health benefits should be less than 5% - approximately 25 grams, or six teaspoons of sugar (WHO, 2019). Ultra-processed foods are not 'real food'. As stated, they are formulations of food substances often modified by chemical processes and then assembled into ready-to-consume hyper-palatable food and drink products using flavors, colors, emulsifiers and a myriad of other cosmetic additives. Most are made and promoted by transnational and other giant corporations. Their ultra-processing makes them highly profitable, intensely appealing and intrinsically unhealthy (Monteiro et al, 2018).

1.3 Popularity and trend

Ultra-processed foods (UPFs) are now simply part of modern life. As they are convenient, affordable, profitable and flavored, they are eaten in many countries and are on sale everywhere. These foods are now account for more than half of all the calories eaten by the population (Wilson, 2020). Studies report that ultra-processed foods already make up more than half of the total dietary energy consumed in high-income countries such as the USA, Canada and the UK and between one-fifth and one-third of total dietary energy in middle-income countries such as Brazil, Mexico and Chile. The average growth in sales of these products amounts to about 1% per year in high-income countries and up to 10% per year in middle-income countries (Monteiro et al, 2018).

1.4 Processed Foods and Health risks

For many years, diet and nutrition experts have been warning the public to avoid consuming too much processed food. Cancer Prevention Recommendations asked to limit the amount of red and processed meat we eat (Wilson, 2020). Elizabeth et al (2020) reviewed the relevant studies in investigating the associations between levels of UPF consumption and health outcomes. Of 43 studies reviewed, 37 found dietary UPF exposure associated with at least one adverse health outcome.

Many of health issues related to ultra-processed food. Studies have shown that diets high in ultra-processed food tend to be connected with a higher risk of chronic disease. In addition, there has been at least one massive study that links excessive consumption of ultra-processed foods with increased cancer risk. Studies found strong evidence that a Western diet, is related to weight gain. The overweight and obesity are a cause of at least 12 types of cancer (Croker, 2022). Fiolet et al (2018) studied the prospective associations between consumption of ultra-processed food and risk of cancer. It was reported that a 10% increase in the proportion of ultra-processed foods in the diet was associated with a significant increase of greater than 10% in risks of overall and breast cancer. Rauber et al (2018) described the contribution of ultra-processed foods in the U.K. diet and its association with the overall dietary content of nutrients known to affect the risk of chronic non-communicable diseases (NCDs).

Other previous research found that people who consumed more ultra-processed foods had higher risks of cardiovascular disease, coronary heart disease, and cerebrovascular disease. Although large observational studies do not prove cause and effect, the research does suggest an association between ultra-processed diets and heart disease (Srour et al, 2019).

Moreover, there is another evidence that links ultra-processed foods with a range of health risks (Lawrence and Baker, 2019). It was found that there were positive associations between consumption of ultra-processed foods and risk of cardiovascular disease and death.

Over the past decade, large-scale studies from France, Brazil, the US and Spain have recommended that high consumption of UPFs is related to higher rates of obesity. Ultra-processed has emerged as the most persuasive new metric for measuring what has gone wrong with modern food (Wilson, 2020). Cardoso et al (2022) evaluate the association between ultra-processed food consumption and cognitive performance in US older adults. The results show that UPF consumption was related to worse performance in older people without pre-existing diseases. Reducing the UPF consumption could be the way to enhance impaired cognition among older adults. No significant vital associations were determined between the UPF intake tertiles and the cognitive test results. Martínez Leo et al (2019) study the effect of ultra-processed diet on gut microbiota and thus its role in neurodegenerative diseases. This study highlights the importance of a search for stricter public health strategies regarding access to and development of ultra-processed foods.

Giromini and Givens (2022) discusses the dietary impact of red and processed meat, with some reference to the relative effect of white meat, in a range of chronic conditions including iron-deficiency anaemia, cardiovascular diseases (CVD), cancer and dementia. The study supported the statement that red meat and especially processed meat are related to increasing risks of CVD, cancer and dementia whereas white meat is neutral a lower risk. The study appears little doubt that processed and unprocessed meat should have separate public dietary guidance.

Several studies suggest that the Mediterranean diet is associated with better global cognition in older adults, slower cognitive decline and lower risk of dementia. Dobreva and Mukadam (2022) used self-reported consumption of food groups, considered part of the Mediterranean diet. The study found the reduction of the risk of dementia in the fish consumption of 2.0 to 3.9 times a week, and also, the fruit consumption of 1.0 to 1.9 servings a day

Ylilauri et al (2022) investigate if dairy, meat, and fish intakes associate with dementia and cognitive performance. The findings show that although higher intake of some food groups associated with cognitive performance, there is little evidence for associations with dementia risk. D'Cunha et al (2022) study the Effects of Dietary Advanced Glycation End-Products on Neurocognitive and Mental Disorders. This study suggests that decreasing dietary intake of AGEs may improve neurological and mental disorder outcomes.

2. Alzheimer's disease and Dementia

Alzheimer's is a specific disease and the most common cause of dementia. Dementia is not. Dementia results from a variety of diseases and injuries that primarily or secondarily affect the brain. Dementia is a decline in mental ability severe enough to interfere with person's daily life and activities such as decline in remembering, reasoning or thinking. 60-80% of dementia cases caused from Alzheimer's disease (Alzheimer Association, 2022b). Dementia is currently the seventh cause of death among all diseases and one of the major causes of disability and dependency among older people globally (WHO, 2021).

Neurodegenerative diseases, including Alzheimer's disease (AD) which are an increasing social, economic and medical problem is resulting in the ageing of the population. The important modifiable factors are Diet and physical activity are considered as that help prevent or delay the development of AD and other dementia-related diseases. (Kępka et al, 2022)

The number of people who living with dementia and Alzheimer's disease is growing rapidly, making dementia one of the biggest challenges for this century. Several studies have indicated that depression plays an important role in development of dementia, including Alzheimer's disease; depression, especially, during the late life may either increase the risk of dementia or even being its prodromal stage (Kuo et al, 2020).

2.1 Definition of Alzheimer's disease

Alzheimer's disease is the most common cause of dementia that affects memory, thinking and behavior. This disease interferes with patients' daily lives. The greatest risk factor is increasing age as the majority of people suffering with Alzheimer's are above 65. This disease is a progressive disease, it will gradually worsen over years (Alzheimer Association 2022).

Alzheimer's disease (AD) dementia refers to a particular onset and course of cognitive and functional decline associated with age together with a particular neuropathology. It was first described by Alois Alzheimer in 1906. In the United States there is a disproportionate disease burden in minority populations (Soria Lopez et al, 2019, De-Paula et al, 2012). There is still no cure for Alzheimer's dementia and available treatment strategies bring only symptomatic benefits, there is a pressing demand for other effective strategies such as diet (Szczechowiak et al, 2019).

2.2 Symptoms

People with Alzheimer's usually have signs of late-onset Alzheimer's in their mid-60s. For the people who have early onset Alzheimer's, the signs usually begin between a person's 30s and mid-60s. The first symptoms vary from person to person. Example of typical signs are memory problems, decline in word-finding skills, vision issues and impaired reasoning. During the progression of the disease, AD patients will experience grater memory loss and other cognitive difficulties (NIA, 2017a).

2.3 Number of Alzheimer's patients

Alzheimer's is on the rise throughout the world. The WHO reported that development of dementia occurs to someone every 3 seconds. There are over 55 million people worldwide living with dementia in 2020. This figure will double every 20 years, reaching 78 million in 2030 and 139 million in 2050. 60% of people with dementia live in low- and middle-income countries, but will rise to 71% by 2050. The fastest growth in the elderly population is taking place in China, India, and their south Asian and western Pacific neighbors (WHO, 2020).

2.4 Alzheimer's Risk Factors

Age is a main risk factor of Alzheimer's disease (AD); however, there are also other risk factors. The genetic variant of the Apolipoprotein E (APOE) gene on chromosome 19 does increase a person's risk, even though the specific genes that caused late onset Alzheimer's are still not found. An exposure to chemicals and brain injury can increase the risk of Alzheimer's, dementia and Parkinsonism. Physical and mental activities and psychological stress are possible factors. Nutrition can prevent and also worsen the symptoms. Potential environmental risk factors being investigated include secondhand smoke, air pollution and pesticides (NIA, 2017b). Additional risk factors include depression, social isolation, low educational attainment, cognitive inactivity and air pollution (WHO, 2021). Previous studies show that people can reduce their risk of cognitive decline and dementia by being physically active, not smoking, avoiding harmful use of alcohol, controlling their weight, eating a healthy diet, and maintaining healthy blood pressure, cholesterol and blood sugar levels.

2.5 Studies on the Associations between Ultra-processed Foods and Dementia

According to a new study (American Academy of Neurology, 2022). Li et al. (2022) found that replacing ultra-processed foods in a person's diet with unprocessed or minimally processed foods was associated with a lower risk. People who eat the high amounts of ultra-processed foods like soft drinks, chips and cookies may have a higher risk of developing dementia than those who eat the low amounts. This study did not prove that ultra-processed foods cause dementia.

Ultra-processed foods have been shown in other studies to have negative effects on thinking and memory skills. Their research not only found that ultra-processed foods are associated with an increased risk of dementia, it found replacing them with healthy options may decrease dementia risk. Researchers found that for every 10% increase in daily intake of ultra-processed foods, people had a 25% higher risk of dementia (Li et al 2022).

However, Alzheimer's Research UK said it was unclear why ultra-processed food was driving the increased risk, but said it could be that diets involving lower levels of important nutrients such as fibre or may lead to high blood pressure or inflammation, which can be bad for long-term brain health said Dr Sara Imarisio, the head of research at Alzheimer's Research UK (Knapton, 2022). Another evidence, which using the same database suggested that keeping physically and socially active is likely to have the greatest benefit to health, rather than the activity itself. The researchers also found that even people with a high genetic risk for Alzheimer's, could benefit from keeping physically active (Jianwei et al 2022).

Other study (Samieri et al, 2020) used network science tools to identify novel diet patterns in prodromal dementia. Their findings show how foods are consumed (and not only the quantity consumed) may be important for dementia prevention. The worse eating habits toward charcuterie and snacking, were evident years before diagnosis in this cohort. Network methods, which are designed to model complex systems, may advance our understanding of risk factors for dementia. Zhang et al, (2021) investigate associations between meat consumption and risk of incident dementia in the UK Biobank cohort. The short dietary questionnaire was used to estimate the meat consumption at recruitment and repeated 24-h dietary assessments. These findings highlight processed-meat consumption as a potential risk factor for incident dementia. Mercer (2019) reported Australian study which links Fast Food and dementia. The Australian National University (ANU) gave the warning about the extra calories in a fast-food and brain diseases, including dementia. The ANU study also finds the link between type 2 diabetes, which is often triggered by obesity, and the rapid deterioration of brain function. Dementia is the number one cause of death in Australian women, while for men it is second only to heart disease.

2.6 Studies the Associations between Alzheimer's disease and ultra-processed food

Even though scientists used to think that the disease is caused by genetic, in fact, the genetic mutation is only one percent cause and the rest are other conditions including behavioral and lifestyle factors. Researchers think that one third of AD cases could be prevent by improving the lifestyles. One way of improvement is eating better which means that processed food should be cut out as much as possible (Pathways Home Health and Hospice, 2022). Eating less of healthy foods and many complex carbohydrates, processed foods and sugar can stimulate the production of toxins resulting in inflammation. Moreover, overall cognitive function might be impaired by the plaques in the brain.

Więckowska-Gacek et al. (2021) suggested that western diet-evoked memory impairment and AD hallmarks in the brain. Western diet (WD) defines as a modern pattern of nourishment typical for western societies, based on ultra-processed foods, made from refined substances, rich in simple carbohydrates (sugars), salt, saturated fats (SFA) and cholesterol. It is also poor in grain and fiber. Moreover, WD significantly affects the functioning of the gut and the gut commensal microbiota, thereby indirectly leading to a reduction in the absorption of nutrients and vitamins supplied with food (Christ and Latz., 2019; Lustig, 2020). Most commonly diets with 35%–60% of fat with high concentration of SFA and additional amounts of simple sugar and cholesterol are used.

Ultra-processed foods and some culinary techniques represents the main sources and the drivers of dietary AGEs (Advanced glycation end products) which are glycated protein or lipids formed in human body or consumed through diet. The studies show that AGEs were associated with high incidence of cognitive impairment in the elderly. AGEs show significant toxicity in cortical neuronal cells and the presence of AGEs was demonstrated in AD patient. AGEs can develop dementia by causing the loss of cerebral pericytes in vascular dementia and neuronal cell apoptosis. A high concentration of AGEs is contained in products that consist of large quantity of sugar, trans-fat, processed dairy products and fast food (D'Cunha et al, 2022).

2.7 Alzheimer's disease and Healthy diet

The evidence from the observations shown the patients whose cognitive decline was reversed after making specific lifestyle changes, including changing their diet (Prime Health 2022). Previous study also suggested that diet is considered as important factors that help prevent or delay the development of Alzheimer's disease and other dementia-related diseases. The consumption of vegetables, fruits, vegetable oils and fishes are recommended while processed food are prohibited. Limited in consumption of animal fats, having fruits and nuts instead of sugar and sweets, and should not add salt to foods (Solfrizzi et al, 2011a). Moreover, recent studies provided evidence that higher adherence to a Mediterranean-type diet (MeDi) could be associated with slower cognitive decline, reduced risk of AD, and decreased all-causes mortality in AD patients. These findings suggested that adherence to the MeDi may affect not only the risk for AD, but also for predementia syndromes and their progression to overt dementia (Solfrizzi et al, 2011b).

Diet and physical activity are now considered as important modifiable factors that help prevent or delay the development of AD and other dementia-related diseases. The nutritional recommendations for healthy adults primarily include the consumption of vegetables, fruits, cereals, legumes, vegetable oils and fishes. Therefore, the introduction of Mediterranean and Asian diets may reduce the risk of the neurodegenerative diseases associated with dementia, whereas dairy products and meat-the main sources of L-carnitine-should be consumed in moderate amounts (Kepka et al, 2022).

IV. DISCUSSION OF THE RESULTS

From the review of the literature, it can be categorized issues related to ultra-processed food and Alzheimer's disease as shown in the Table 1 to Table 4. First, as presented in Table 1, it suggests that ultra-processed food is associated with at least one adverse health outcome. There is an association between ultra-processed diets and heart disease and a significant increase of greater than 10% in risks of overall and breast cancer, and the risk of chronic non-communicable diseases (NCDs). Previous studies also suggested that there is the association between ultra-processed food consumption and cognitive performance in US older adults. Table 2 reported the studies on the association between ultra-processed food and dementia. These studies suggested that the higher consumption of UPF was associated with higher risk of dementia, while substituting unprocessed or minimally processed foods for UPF was associated lower risk of dementia. The research highlighted processed-meat consumption as a potential risk factor for incident dementia. Table 3 reported the studies on the association between ultra-processed food and Alzheimer's disease in particular. It was reported that ultra-processed foods represented the main sources and drivers of dietary AGEs. Tissue accumulation of AGEs has been associated with cellular aging and implicated in various age-related diseases, including type-2 diabetes and cardiovascular disease. Adding sugar,

and by proxy the ultra-processed food category, also meets the four criteria set by the public health community as necessary and sufficient for regulation-abuse, toxicity, ubiquity, and externalities. Moreover, as a modern pattern of nourishment typical for western societies based on ultra-processed foods based on ultra-processed foods, western diet-evoked memory impairment and Alzheimer's disease hallmarks in the brain. Table 4 presents that there is the evidence that diet and physical activity are now considered as important modifiable factors that help prevent or delay the development of AD and other dementia-related diseases.

Table 1: Review of the studies about processed foods and health risks

Authors	Research titles	Findings
Processed foods and Health risks		
Srour et al (2019)	Ultra-processed food intake and risk of cardiovascular disease: prospective cohort study	There is an association between ultra-processed diets and heart disease.
Elizabeth et al (2020)	Ultra-Processed Foods and Health Outcomes: A Narrative Review.	The dietary UPF exposure is associated with at least one adverse health outcome.
Fiolet et al (2018)	Consumption of ultra-processed foods and cancer risk: results from NutriNet-Santé prospective cohort	A 10% increase in the proportion of ultra-processed foods in the diet was associated with a significant increase of greater than 10% in risks of overall and breast cancer.
Rauber et al (2018)	Ultra-Processed Food Consumption and Chronic Non-Communicable Diseases-Related Dietary Nutrient Profile in the UK (2008-2014)	The contribution of ultra-processed foods in the U.K. diet and its association with the overall dietary content of nutrients known to affect the risk of chronic non-communicable diseases (NCDs).
Cardoso et al (2022)	Association between ultra-processed food consumption and cognitive performance in US older adults: a cross-sectional analysis of the NHANES 2011-2014	There is the association between ultra-processed food consumption and cognitive performance in US older adults. No significant vital associations were determined between the UPF intake tertiles and the cognitive test results
Martínez Leo et al (2019)	Effect of ultra-processed diet on gut microbiota and thus its role in neurodegenerative diseases	The effect of ultra-processed diet on gut microbiota and thus its role in neurodegenerative diseases.
Giromini and Givens (2022)	Benefits and Risks Associated with Meat Consumption during Key Life Processes and in Relation to the Risk of Chronic Diseases	The study supported the statement that red meat and especially processed meat are related to increasing risks of CVD, cancer and dementia whereas white meat is neutral a lower risk.

Table 2: Review of the studies about Ultra-processed foods and Dementia

Authors	Research titles	Findings
Ultra-processed Foods and Dementia		
Li et al. (2022)	Association of Ultra-processed Food Consumption With Risk of Dementia A Prospective Cohort	The higher consumption of UPF was associated with higher risk of dementia, while substituting unprocessed or minimally processed foods for UPF was associated lower risk of dementia.
Zhang et al (2021)	Meat consumption and risk of incident dementia: cohort study of 493,888 UK Biobank participants.	Highlight processed-meat consumption as a potential risk factor for incident dementia.

Table 3: Review of the studies about Ultra-processed Foods and Alzheimer's disease

Authors	Research titles	Findings
Ultra-processed food and Alzheimer's disease		
Więckowska-Gacek et al (2021)	Western diet as a trigger of Alzheimer's disease: From metabolic syndrome and systemic inflammation to neuroinflammation and neurodegeneration	Western diet-evoked memory impairment and AD hallmarks in the brain.
Lustig (2020)	Ultraprocessed Food: Addictive, Toxic, and Ready for Regulation	There is the evidence that added sugar, and by proxy the ultraprocessed food category, meets the four criteria set by the public health community as necessary and sufficient for regulation-abuse, toxicity, ubiquity, and externalities
D'Cunha et al (2022)	The Effects of Dietary Advanced Glycation End-Products on Neurocognitive and Mental Disorders.	Ultra-processed foods represent the main sources and drivers of dietary AGEs. Tissue accumulation of AGEs has been associated with cellular aging and implicated in various age-related diseases, including type-2 diabetes and cardiovascular disease.

Table 4: Review of the studies about Alzheimer's disease and healthy diet

Authors	Research titles	Findings
Alzheimer's disease and Healthy diet		
Kępka et al (2022)	Healthy Food Pyramid as Well as Physical and Mental Activity in the Prevention of Alzheimer's Disease	Diet and physical activity are now considered as important modifiable factors that help prevent or delay the development of AD and other dementia-related diseases.

V. FUTURE RESEARCH

Future research should explicitly explore the associations between ultra-processed food and health harms related to Alzheimer's disease. In the meantime, policy makers should shift their priorities away from food reformulation which risks positioning ultra-processed food as a solution to dietary problems towards a greater emphasis on promoting the availability, affordability, and accessibility of unprocessed or minimally processed foods.

VI. CONCLUSION

The rise of Alzheimer's patients has increased from time to time which related to people are living longer. The age is the preeminent risk factor for Alzheimer's disease, which spells trouble for families and healthcare systems. However, age is inevitable but dementia is not. It's important to note that several studies do not prove that ultra-processed foods cause dementia or Alzheimer's. It only shows the association between them. However, that ultra-processed foods represented the main sources and drivers of dietary AGEs. Tissue accumulation of AGEs has been associated with cellular aging and implicated in various age-related diseases. There is an association between ultra-processed diets and heart disease and a significant increase of greater than 10% in risks of overall and breast cancer, and the risk of chronic non-communicable diseases (NCDs). In this study, it should be considered as important to gain a better understanding of Alzheimer's disease pathogeneses. It is beneficial to discuss the evidences of recently established interventions considered to prevent or delay the prodromes of dementia and Alzheimer's disease and provide the prospective future directions in prevention and management of dementia and Alzheimer's disease. Diet is considered as important factors that help prevent or delay the development of Alzheimer's disease and other dementia-related diseases. Preventing or postponing the onset of Alzheimer's disease (AD) and delaying its progression would lead to an improvement of health status and quality of the older age life.

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