



Review

Alzheimer's Disease Prevention - A Review of Modifiable Risk Factors and the Role of Dietary Supplements

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Abstract

Alzheimer's disease is a prevalent age-related medical problem world-wide for which there is no cure. Over the past few decades, researchers have identified 14 potentially modifiable risk factors for this disease. They include physical inactivity, unhealthy diet, and cardiovascular risk factors such as hypertension, hyperlipidemia, diabetes mellitus and smoking. It is estimated that a third of Alzheimer's disease cases can be prevented by addressing risk factors at an earlier age. In addition, available data suggest that some dietary supplements may be helpful in preventing or treating dementia, though further high quality studies are needed.

Keywords: Dementia prevention; Dietary supplements; Modifiable risk factors; Prevention of Alzheimer's disease

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Introduction

Alzheimer's Disease (AD) is a prevalent age-related health care problem for which no curative treatment is available. It is estimated that approximately 45 million people in the world suffer from dementia. AD accounts for the vast majority (up to 80%) of dementia cases [1]. Systematic reviews of population-based studies have shown evidence of decreasing prevalence of dementia in Europe and North America over the past 2-3 decades [2]. This observed decline is likely related to improved control of cardiovascular risk factors and to higher rates of early-life educational achievement. This evidence strengthens the belief that age-related dementia can be preventable. It is estimated that a third of AD cases are potentially ascribable to modifiable risk factors [3].

The World Health Organization regards dementia prevention as a public health priority [4]. Improved understanding of preventive strategies could help abate the enormous socioeconomic burden of this disease and make a significant difference in the lives of millions of people worldwide [5,6]. In this review, we focus our discussion around the potentially modifiable risk factors for AD. We comment on available evidence-based strategies for possible AD prevention. In addition, we review the literature regarding the role of dietary supplements in the prevention of AD.

Risk Factors for Alzheimer's Disease

Modifiable: Physical inactivity; mental inactivity; unhealthy diet; hypertension; diabetes mellitus; hyperlipidemia; smoking; obesity; traumatic brain injury; sleep disorders; depression; chronic periodontitis; hearing loss; herpes viral infection.

Non-modifiable: Age and Genetics.

Modifiable risk factors

Physical inactivity

As shown in human studies, physical exercise has important benefits to the cerebral structure and function. It promotes neuroplasticity or brain malleability which is the brain's ability to modify itself when adjusting to environmental changes [7]. Physical exercise helps maintain brain volume including gray matter volume in the frontal and hippocampal regions [8,9]. It promotes increased levels of neurotrophic factors namely peripheral Brain-Derived Neurotrophic Factor (BDNF). This effect has been observed in at least five randomized controlled trials involving elderly patients who participated in moderate-intensity exercise training [10]. BDNF stimulates brain cells to grow and survive. In addition, this neurotrophic factor induces brain cells to create compensatory mechanisms when facing insults such as disease or injury. Moreover, physical exercise improves cerebral blood flow and the transport of vital ingredients to brain cells.

We will briefly discuss the results of a few studies which highlight the importance of physical exercises in the prevention of dementia: Physical exercise is associated with enhanced cognitive abilities and

reduced risk of developing dementia in the elderly. A recent meta-analysis examined the effects of exercise training on cognitive function in individuals considered at risk of or who have AD [11]. This analysis included 1,145 subjects from nineteen studies with a mean age of 77. Participants were considered at risk of AD if they had Mild Cognitive Impairment (MCI), a genetic risk such as apolipoprotein E4 allele, or a parent diagnosed with AD. On average, the interventions consisted of moderate intensity physical exercises, mainly aerobic type, 45 minutes per session, 3 days per week, for 18 weeks. The results indicate meaningful improvements in cognitive function with aerobic exercise training. The authors conclude that exercise training may slow the gradual cognitive decline that is normally expected in these individuals. More specifically, this study identifies aerobic exercise as being superior to other exercise modalities in preserving cognitive function [12] (Table 1).

The best time in life for obtaining the most protective brain benefits from physical activity remains unclear. Midlife appears to be a vulnerable period when the effects of cardiovascular risk factors contribute to the development of dementia in later life [6,13]. Investigators from Sweden recently published the results of their study evaluating the association of midlife cardiovascular fitness and dementia. It was a 44-year longitudinal population study in Swedish women. They concluded that high cardiovascular fitness in midlife appears to reduce the risk of developing dementia in later life [14] (Table 1).

Interestingly, physical activity appears to confer better neurocognitive protection to individuals considered at risk of developing AD such as APOE-epsilon 4 allele carriers [15]. Hippocampal atrophy is a typical brain imaging finding of AD which gradually worsens with disease progression. It may also be associated, to a lesser degree, with normal aging. Erickson et al., in 2011 showed the effectiveness of physical activity in improving hippocampal volume as well as cognitive function in healthy older adults [16]. Another study in 2014 evaluated 97 healthy older adults with brain MRI scans at baseline and following 18-month-long physical activity training. Participants were involved in either Low intensity Physical Activity (Low PA) or High intensity Physical Activity (High PA). Individuals who had the APOE-epsilon 4 allele received the high risk status. The study participants were divided into four distinct intervention groups: Low Risk/High PA, Low Risk/Low PA, High Risk/High PA and High Risk/Low PA. The follow-up brain MRI scans revealed a 3% decrease (worsening) in hippocampal volume in the High Risk/Low PA group but was unchanged in the High Risk/High PA and other two groups. The results suggest that physical activity may help decrease hippocampal atrophy in individuals at higher genetic risk of developing AD [15] (Table 1).

Unhealthy diet

Certain dietary practices have been increasingly recognized as effective measures in the prevention of cognitive decline. Most observational studies have linked the Mediterranean Diet (MD) to a lower incidence of all-cause dementia [17]. This diet may provide brain protection by reducing oxidative stress and inflammation [18]. The MD is characterized by a high intake of fruits, vegetables, legumes, nuts, seeds, beans, whole grains, fish with omega-3 fatty acids (salmon, tuna and mackerel) and olive oil. Poultry, dairy products, eggs and wine are consumed in moderation. The MD is typically low in sources of saturated fats such as red meat and butter [19]. A systematic review of the literature in 2016, concluded that adherence to the MD is associated with improved cognitive function. Nevertheless, the authors cautioned that most of the data originated from epidemiologic studies and not from controlled trials [20].

The PRIMED-NAVARRA study is the largest randomized clinical trial to date assessing the effects of the MD on cognition [21]. This study evaluated 522 participants, mean age 74 years, who were considered at high risk for vascular disease. Individuals were randomly assigned to one of three diet groups: MD supplemented with extra-virgin olive oil, MD supplemented with mixed nuts or low-fat control diet. The authors administered neuropsychological testing at baseline and after a mean follow-up of 6.5 years. Participants who adopted the two types of the MD had significantly higher mean scores on follow-up neuropsychological testing (Table 2).

Valls-Pedret et al., investigated whether a MD supplemented with either extra virgin olive oil or mixed nuts affects cognitive function compared with regular diet. This study evaluated 447 cognitively normal older patients at high cardiovascular risk. At the end of 4 years, the two MD groups showed improved cognitive function compared to the control group [22] (Table 2). The MIND (Mediterranean-DASH Intervention for Neurodegenerative Delay) diet is a hybrid of the Mediterranean and the DASH (Dietary Approaches to Stop Hypertension) diets. This diet emphasizes the increased consumption of berries as well as green leafy vegetables (such as collard greens, spinach, and kale). The MIND diet does not specify increased consumption of fruits, potatoes, dairy, or more than one fish meal per week [23]. The MIND diet study was a prospective trial investigating the relations of three distinct diets and the risk of developing AD [24]. The authors evaluated 923 participants who were following either the MIND, the DASH or the Mediterranean diet. This five-year-long study showed that high adherence to all three diets was associated with a reduced AD risk. Notably, even moderate adherence to the MIND diet was associated with a decreased AD risk [24] (Table 2).

	Gregory A. Panza et al.,	Helena Horder et al.,	J. Carson Smith et al.,
Number of participants	1,145, most of them at risk of AD	191 (women)	97
Mean age	77	50	72
Study design	Meta-analysis	Longitudinal, observational, cohort	Longitudinal, cohort
Intervention	Controlled studies that included a physical exercise intervention	Evaluation of cardiovascular fitness in midlife	High-physical exercise intervention
Control group	Nondiet, nonexercise, group	Lower cardiovascular fitness	Low-physical exercise group
Outcomes	Change in cognitive performance	Change in cognitive performance	Change in hippocampal volume
Findings	Exercise training may delay the decline in cognitive function	High cardiovascular fitness in midlife is associated with decreased risk of subsequent dementia	Increased physical exercise may help decrease hippocampal atrophy in individuals at high risk of AD

Table 1: Summary of studies on the effects of physical exercise on cognitive function.

	Martinez-Lapiscina et al., (PRIDIMED-NAVARRA study)	Valls-Pedret et al.,	Morris et al.,
Number of participants	522	447	923
Mean age	74	67	81
Study design	Parallel-group, randomized	Parallel-group, randomized	Prospective, observational
Intervention	Dietary (MD, 2 sub-types)	Dietary (MD, 2 sub-types)	Dietary (MIND, DASH, or MD)
Control group	Low-fat diet	Regular diet	n/a
Outcomes	Change in cognitive performance	Change in cognitive performance	Change in cognitive performance
Findings	My may improve cognition	My may improve cognition	High adherence to all 3 diets may improve cognition Moderate adherence to the MIND diet may improve cognition

Table 2: Summary of studies on the effects of dietary changes on cognitive function.

Mental inactivity

Epidemiological studies have suggested a reduced risk of developing AD in individuals with higher educational/occupational attainment as well as higher exposure to stimulating social environments [25]. These individuals develop the so-called “cognitive reserve” which helps them maintain normal cognitive function for longer when their brains are undergoing structural changes related to AD. It is plausible that intellectual activities create cognitive reserve by promoting neurogenesis [26] and stimulating neurotrophic factors such as peripheral Brain-Derived Neurotrophic Factor (BDNF). As mentioned earlier, BDNF provides brain protection by promoting neuroplasticity as a compensatory reaction to brain insults [27]. A prospective, population-based cohort study in 2017 evaluated the association of mentally stimulating activities in old age with neurocognitive function. The authors followed 1929 cognitively normal individuals 70 years or older for 4 years. Participants who engaged in various intellectual activities including regular computer use, craft activities, social activities and playing games showed significant decreased risk of new-onset mild cognitive impairment [28].

Vascular Risk Factors: Hypertension, Hyperlipidemia, Diabetes, Smoking, Obesity

Observational studies over the years have shown a link between vascular risk factors and AD. Hypertension, hyperlipidemia, diabetes, obesity and smoking, alone or in combination, can cause damage to the cerebral blood vessels and might contribute to the development of AD. A recent original investigation concluded that having vascular risk factors in midlife contributes to brain amyloid deposition in late-life [29]. This prospective cohort study evaluated 346 participants without dementia, mean age of 52, for vascular risk factors including hypertension, diabetes, total cholesterol >200 mg/dL, current smoking and BMI >30. Positron Emission Tomography (PET) was used to detect brain amyloid deposition in late-life, mean age of 76. The results revealed a clear association between an increasing number of vascular risk factors in midlife, but not in late-life, and elevated brain amyloid deposition [29].

Hypertension

High blood pressure appears to contribute to dementia by damaging the brain blood vessels and causing a disruption of the blood-brain barrier. This may lead to protein extravasation and accumulation of amyloid B in the brain tissue [30].

Diabetes mellitus

Diabetes Mellitus has been linked to an increased risk of dementia, including AD [31,32]. Brain dysfunction in the setting of diabetes appears related to increased inflammation and oxidative stress leading to accelerated brain ageing [33]. In addition, hyperinsulinemia may increase amyloid deposition in the brain by impairing its brain clearance mechanisms [34].

Hyperlipidemia

Hyperlipidemia is a well-established risk factor for cerebral vascular disease and has also been associated with AD [35,36]. A recent study from the University of Cambridge identified a specific microscopic pathway by which cholesterol acts as a major catalyst in the accumulation of amyloid-beta protein in the brain [37]. This newly discovered pathway in the brain could represent a target for potential treatments for AD. It is worth mentioning that lipid-lowering therapies such as the Statin drugs have not yet been shown to lower the risk for AD.

Smoking

Cigarette smoking has been increasingly recognized as a modifiable risk factor for AD [38]. Interestingly, some studies published in 1994 or before signaled to a possible protective role of chronic cigarette smoking against the development of AD. A meta-analysis in 2010 concluded that only the tobacco industry funded studies were associated with a decreased risk [38]. Otherwise, this meta-analysis and other subsequent studies indicated an association between cigarette smoking and increased risk for AD [39,40]. Cigarette smoking adversely affects the brain by causing a state of chronic oxidative stress which may trigger pathophysiological changes of AD [41].

Obesity

Obesity, defined as Body Mass Index (BMI) >30 kg/m², in mid-life is considered a risk factor for AD [42]. Obesity may increase the risk of AD by itself or by leading to other known risk factors such as hypertension, diabetes and hyperlipidemia. According to studies, adipose tissue secretes pro-inflammatory cytokines and causes chronic local and systemic inflammation [43]. Chronic brain inflammation leads to abnormal cerebral insulin action which may contribute to amyloid B and tau protein accumulation [44].

Traumatic brain injury

For many years, moderate to severe traumatic brain injury, has been considered a risk factor for earlier onset AD [45,46]. Traumatic

brain injury may increase dementia risk by causing brain atrophy, white matter degeneration and neuroinflammation. A recent retrospective study examined the association between traumatic brain injury severity and dementia diagnosis. The authors found a 2-fold increase in dementia diagnosis associated with mild traumatic brain injury without loss of consciousness [47]. This finding highlights the importance of proper brain protection against trauma in at risk situations including the practice of contact sports.

Sleep disorders

Sleep disorders are known for disturbing memory consolidation processes in the brain and therefore leading to learning difficulties [48]. It is also known that individuals who suffer from sleep disorders are more likely to receive a diagnosis of AD [49]. To this date, it is unclear whether abnormal sleep patterns play a causal role in the pathophysiology of AD or whether they represent early clinical manifestations of this degenerative brain disorder [50]. A systematic review and meta-analysis in 2016 quantified an "average" magnitude of the association between sleep disorders and AD [51]. According to this meta-analysis, individuals with sleep disorders are 1.68 times more likely to have cognitive impairment and/or AD. Their findings suggest that 15% of AD cases may be attributed to sleep problems.

Depression

AD is often accompanied by major depressive disorder [52] and the appearance of depressive symptoms in older age may represent a prodromal manifestation of dementia [53]. In addition, studies have shown that major depressive disorder in mid-life is considered an independent risk factor for AD [54]. The exact mechanism of this association is unknown but may be related to raised cytokines, increased brain inflammation and aberrant hypothalamic pituitary axis function [55].

Chronic periodontitis

Studies have linked chronic periodontitis to several inflammatory conditions, cardiovascular disease [56] and neurodegenerative disease [57]. Chronic periodontitis is associated with increased levels of pro-inflammatory markers including C-reactive protein [58]. It may play a role in the pathogenesis of AD by increasing brain inflammation and triggering vascular dysfunction. A retrospective cohort study in 2017 demonstrated that 10-year chronic periodontitis exposure increased the risk of developing AD by 1.7 [59]. These results call attention to the need for improved prevention and treatment of periodontal disease.

Hearing loss

Hearing impairment has been increasingly considered as a risk factor for AD [60,61]. The mechanisms of this association are unclear but may relate to social isolation which is a known contributor to dementia. Hearing loss has also been shown to adversely affect cognition by diverting cognitive resources from working memory toward improved auditory processing [62]. A systematic review in 2017 evaluated an association between hearing loss and dementia. The several studies in this review utilized different evaluation methods but they all demonstrated a link between hearing loss and dementia in older adults [63]. High-quality prospective studies are needed to confirm this association. In the meantime, we should continue efforts to detect and treat hearing impairment for improved socialization and quality of life as well as for possible prevention of cognitive decline.

Viral infection

Recent studies suggest a link between brain infection with herpesviruses and AD [64-66]. Investigators detected more signs of active viral infection in postmortem brains of individuals who had AD compared to controls [64]. Herpes viral infection appears to trigger an accelerated deposition of beta amyloid protein in the brain as a protective measure against viral cell damage [65]. A retrospective cohort study from Taiwan in 2018 investigated the association between herpes simplex viral infection and dementia as well as the possible effects of anti-herpetic medications in attenuating this risk. The results suggest that patients with herpes simplex viral infection may have a 2.56-fold increased risk of dementia. Notably, the use of anti-herpetic medications was associated with a decreased risk of dementia [67]. More research is needed to clarify the relationship between herpesviruses and AD and the role of antiviral medications.

Dietary Supplements for Alzheimer's Disease Prevention

Vitamins

Vitamin D

Several recent meta-analyses and systematic reviews have confirmed the association between low vitamin D levels and an increased risk for dementia, poor cognitive performance, and cognitive decline [68-71]. In one meta-analysis, a decreased risk of dementia was seen at serum levels of at least 25ng/ml [68]. In another, patients with serum levels below 20ng/ml had a 21% higher risk of developing Alzheimer's disease than did those with higher levels [71]. While epidemiologic data do seem to support vitamin D's role in the prevention of dementia, interventional studies have been sparse and have failed to show a benefit with supplementation [69]. Clinicians can advise their patients that until further studies are done, maintaining a vitamin D level of at least 20ng/ml may be helpful in reducing their risk of AD and dementia.

Vitamin E

While a 2017 Cochrane systematic review found no evidence that vitamin E improves cognition or prevents progression to dementia in patients with MCI, some earlier studies did have positive findings [72]. A 1997 RDBPCT found that in patients with moderately severe AD, 2000 IU/day of vitamin E delayed disease progression [73]. A later study showed that when patients with mild to moderate AD were given the same dose of vitamin E, they retained their ability to perform ADLs 6 months longer than those given placebo [74]. Providers can inform their patients that vitamin E may be helpful in delaying disease progression and functional decline in those with AD, but it does not appear to prevent progression in those with MCI.

B-Vitamins

While a 2017 meta-analysis failed to show that B-vitamins improve cognition in patients with dementia, earlier studies have been more promising [75]. Supplementation with vitamins B12, B6 and folic acid has been found to decrease cerebral atrophy in cortical regions known to be specifically vulnerable in AD [76]. This effect, however, was only seen in patients with high homocysteine levels at baseline. Similarly, supplementing with these three B-vitamins decreased cognitive decline in patients with MCI and elevated homocysteine levels

[77]. Interestingly, some data show that omega-3 fatty acids are a necessary co-requisite in achieving these cognitive benefits. In patients with MCI who also had low omega-3 fatty acid levels, B-vitamin treatment failed to slow cognitive decline [78]. Similarly, B-vitamin supplementation reduced brain atrophy only in patients with high levels of omega-3 fatty acids [79]. While the data is mixed, the take-home message seems to be that in patients with low to low-normal B12 levels and/or high homocysteine levels, supplementing B12, possibly in combination with folic acid and B6, may help preserve cognitive function, particularly when intake of omega-3 fatty acids is optimal.

Botanicals

Ginkgo biloba

While studies have been inconsistent and often plagued by industry sponsorship, a recent overview of systematic reviews found that *Ginkgo biloba* did have positive effects on cognitive performance, ADLs and clinical global impression in patients with dementia [80-82]. This herb, however, does not seem to be effective for prevention [83]. If patients with established dementia do choose to try *Ginkgo*, providers should recommend the use of at least 200mg per day for at least 22 weeks before determining efficacy [82].

Green tea

Several studies have found a significantly decreased incidence of dementia with green tea consumption [84,85]. This effect seems to be particularly notable in those at an increased risk of developing AD [86]. Among carriers of the ApoE4 gene, regular tea consumption (green, black, and oolong) reduced the risk of cognitive decline by 86% [86]. Green tea consumption, however, does not seem to improve cognition among those who are already cognitively impaired [87]. If patients enjoy drinking green tea, clinicians can encourage them to continue as it may have a protective effect, particularly for those at an increased risk for developing AD.

Resveratrol

Resveratrol has been postulated to improve cognition by optimizing circulation in the brain [88]. Studies in animals have been promising. In rodent models of AD, resveratrol was found to have a neuroprotective effect, improving memory and decreasing amyloid burden in the brain [89]. When studied clinically, results have been mixed. One randomized, placebo-controlled trial did show that resveratrol supplementation modestly improved cognitive performance and memory in healthy postmenopausal women, but other studies have not shown a clinical benefit to supplementation [90-92]. A recent meta-analysis concluded that resveratrol had no significant effect on cognitive performance [93]. Overall, the data for resveratrol in improving cognitive functioning is relatively weak.

Curcumin

Curcumin has well-established antioxidant and anti-inflammatory properties. *In vitro*, curcumin has been found to decrease beta-amyloid protein production and to increase its clearance [94,95]. While preclinical studies have been promising, there is currently not enough clinical evidence to recommend curcumin for the prevention or treatment of dementia. In a recent randomized, double-blind, placebo-controlled trial, curcumin had little effect on cognitive function or

decline in a group of cognitively normal older adults [96]. Regarding its efficacy in dementia treatment, a 2014 systematic review found insufficient evidence to support its use in patients with AD [97]. Study authors have noted poor oral bioavailability, underpowered studies and insufficient follow-up periods as limiting factors [97]. Clinicians should advise their patients that while preclinical evidence is promising, additional studies are needed to further evaluate clinical effects.

Other dietary supplements

Omega-3 fatty acids

Fish and omega-3 fatty acids have also been studied on their own for their role in preventing dementia. In a recent meta-analysis, higher fish intake was associated with a 36% reduced risk of AD [98]. A 1 serving per week increase in fish consumption has been associated with a 7% decrease in the risk of AD and a 5% decrease in the risk of dementia [99]. Similarly, a 0.1g per day increase in consumption of the omega-3 fatty acid, DHA (but not EPA), was associated with a 14% decreased risk of dementia and a 37% decreased risk of AD [99]. Taken in aggregate, these data suggest that higher dietary intakes of fish and possibly fish oil supplements, may lower the risk of AD. If a fish oil supplement is used, the DHA component may be more beneficial than the EPA component.

Acetyl-L-Carnitine

A meta-analysis of placebo-controlled trials found that when given to patients with MCI or early AD, acetyl-l-carnitine had positive effects on both clinical and psychometric scales [100]. Severity and stage of dementia appear to be important determinants of response to this supplement. A Cochrane systematic review evaluating acetyl-l-carnitine for patients with dementia that was not limited to mild forms or early onset showed that acetyl-l-carnitine had a positive effect on clinical global impression, but not on other objectively measured outcomes [101]. Acetyl-l-carnitine may be modestly beneficial for those with mild, early onset dementia.

Phosphatidylserine

Multiple placebo-controlled trials have shown that bovine cortex-derived phosphatidylserine is effective in treating dementia and age-related cognitive decline [102-106]. This form of animal-derived phosphatidylserine, however, is no longer available given safety concerns, namely contamination and transmission of diseases such as Bovine Spongiform Encephalopathy. Plant-derived phosphatidylserine has also been evaluated and while results were promising in a very small preliminary study, a larger follow up study failed to find a beneficial effect [107,108]. When used in combination with DHA or phosphatidic acid, however, cognitive performance was improved in elderly patients with memory impairment or AD [109,110]. Clinicians can advise their patients that there is currently not enough evidence to recommend plant-derived phosphatidylserine on its own for cognitive impairment. If this supplement is tried, a product that combines phosphatidylserine with DHA or phosphatidic acid should be utilized.

Choline

Certain forms of choline have been found to be helpful in patients with AD. Choline alfoscerate (alpha GPC) at a dose of 400mg TID has been found to improve cognition and global function in patients with mild to moderate AD when used over a period of 6 months [111].

This supplement, when taken with donepezil, also decreased mood symptoms in this patient population [112]. A 2010 meta-analysis found that another form of choline (CDP choline) has positive effects on several cognitive domains [113]. In recent studies, CDP choline improved cognition and slowed progression of dementia when used in conjunction with acetylcholinesterase inhibitors [114,115].

Spermidine

Spermidine is a natural polyamine whose intracellular concentration declines in the human brain with ageing [116]. This substance presumably preserves memory performance by regulating neural mechanisms in the brain [117]. A recent randomized, placebo-controlled, double-blind trial from Germany evaluated the impact of spermidine on memory performance in 30 older adults at risk for dementia [117]. This 3-month-long trial showed improved memory performance in the spermidine group compared to the placebo group. Based on the positive results of this small trial, spermidine supplementation shows promise for the treatment of age-related cognitive impairment and warrants further investigation.

Summary

The identification of these 14 potentially modifiable risk factors for Alzheimer's disease should prompt us to create and implement more effective measures for their prevention and/or treatment. By doing so, we may not only decrease the burden of each risk factor in isolation but may achieve 1/3 reduction of Alzheimer's disease cases. Regarding dietary supplements, the available data suggest that some of them may be helpful in preventing and/or treating dementia, though further high quality studies are needed.

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