Reviews

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Nutrition to Prevent or Treat Cognitive Impairment in Older Adults: A GRADE Recommendation

F. Buckinx[1,2], M. Aubertin-Leheudre[1,2]

1. Department of Exercise Sciences, Université du Québec à Montréal (UQAM), Montréal (Qc), Canada; 2. Centre de Recherche de l'Institut Universitaire de Gériatrie de Montréal (CRIUGM), Montréal (Qc), Canada

Corresponding Author: Aubertin-Leheudre Mylene, Département des Sciences de l'activité physique, Faculté des Sciences, UQAM, Pavillon Sciences Biologiques, SB-4615, 141, Avenue du Président Kennedy, Montréal, Québec, Canada, H2X 1Y4. Email: aubertin-leheudre.mylene@uqam.ca

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Abstract

Aging is associated with cognitive declines leading to mild cognitive impairments or Alzheimer disease. Nutrition appear to protect from aging. Some dietary factors could either increase or protect against cognitive declines. This article aimed to provide GRADE recommendations related to nutrition aspects able to prevent or to treat cognitive impairments. A comprehensive literature review was performed using Medline database. The GRADE approach was used to classify quality of the existing evidence (systematic review or meta-analysis). The GRADE process led us to formulate seven key nutritional recommendations to manage cognitive declines, but did not allow us to do it for protein, vitamin B or antioxidants. Thus, 1) adherence to a Mediterranean diet (GRADE 1B); 2) high-level of consumption of mono- or poly- unsaturated fatty acids combined to a low consumption of saturated fatty acids (GRADE 1B); 3) high consumption of fruits and vegetables (GRADE 1B); 4) higher vitamin D intake (GRADE 1C) than the recommended daily allowance. In addition, a ketogenic diet, a low consumption of whole-fat dairy products or a caloric restriction are promising nutritional habits although the evidence does not yet support widespread uptake (GRADE 2C). In conclusion, nutrition is an important modifiable factor to prevent or protect against cognitive decline. Nevertheless, more studies are required to determine specific guidelines such as duration and amounts of nutrients to help older adult to maintain a healthy cognitive life.

Key words: GRADE process, aging, diet guidelines, cognitive impairment.

Introduction

Cognitive impairment is a public health problem due to its increasing prevalence in the aging population (1). It is estimated that 24.3 million people are affected by dementia worldwide, with 4.6 million new cases annually (2). Despite pharmacological advances, there are not yet effective treatments to delay or reverse cognitive impairment (3). Moreover, there is limited knowledge of Alzheimer disease (AD) modifiable risk factors. One of these factors is nutrition (4). According to the World Health Organization (WHO), good nutrition - an adequate, well-balanced diet - is a cornerstone of good health. Immunity system, disease, physical and mental development can be negatively impacted by poor nutrition (5). Therefore, the role of nutrition in cognitive health outcomes has been studied. More specifically, nutrition has been investigated in relation to its ability to maintain cognitive function (3). Caloric intake and diet composition seem to have large and lasting effects on cognition (6). There is more and more evidence suggesting the protective role of certain dietary components (e.g., antioxidant or vitamin nutrients, fish, dietary fats) in the risk of age-related cognitive decline and AD. Several systematic reviews of the literature set out to summarize the evidence considering diet as a protective or risk factor for cognitive decline (7-9); however, clear recommendations have not yet been established. In view of these promising data, consensus is needed on the best eating habits to prevent or to treat cognitive impairment. In this sense, the GRADE (Grades of Recommendation, Assessment, Development, and Evaluation) approach guide about the quality of underlying evidences by providing grade strength of recommendations in health field. The GRADE system classifies evidence quality according to factors such as study methodology, consistency and precision of the results or directness of the finding (10). Therefore, this article aimed to grade, classify and provide recommendations for the preferred diet to prevent or to treat cognitive impairment.

Methods

Study design

This literature review aimed to provide recommendations using GRADE classification on the best nutritional habits to prevent or to treat cognitive impairment, through a narrative synthesis.

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Table 1. Classification of Evidence

Grade of Recommendation	Clarity of risk/benefit	Quality of supporting evidence	Implications
1A. Strong recommendation, high quality evidence	Benefits clearly outweigh risk and burdens, or vice versa.	Consistent evidence from well performed randomized, controlled trials or overwhelming evidence of some other form. Further research is unlikely to change our confidence in the estimate of benefit and risk.	Strong recommendations, can apply to most patients in most circumstances without reservation. Clinicians should follow a strong recommendation unless a clear and compelling rationale for an alternative approach is present.
1B. Strong recommendation, moderate quality evidence	Benefits clearly outweigh risk and burdens, or vice versa.	Evidence from randomized, controlled trials with important limitations (inconsistent results, methodologic flaws, indirect or imprecise), or very strong evidence of some other research design. Further research (if performed) is likely to have an impact on our confidence in the estimate of benefit and risk and may change the estimate.	Strong recommendation and applies to most patients. Clinicians should follow a strong recommendation unless a clear and compelling rationale for an alternative approach is present.
1C. Strong recommendation, low quality evidence	Benefits appear to outweigh risk and burdens, or vice versa.	Evidence from observational studies, unsystematic clinical experience, or from randomized, controlled trials with serious flaws. Any estimate of effect is uncertain.	Strong recommendation, and applies to most patients. Some of the evidence base supporting the recommendation is, however, of low quality.
2A. Weak recommendation, high quality evidence	Benefits closely balanced with risks and burdens.	Consistent evidence from well performed randomized, controlled trials or overwhelming evidence of some other form. Further research is unlikely to change our confidence in the estimate of benefit and risk.	Weak recommendation, best action may differ depending on circumstances or patients or societal values.
2B. Weak recommendation, moderate quality evidence	Benefits closely balanced with risks and burdens, some uncertainly in the estimates of benefits, risks and burdens.	Evidence from randomized, controlled trials with important limitations (inconsistent results, methodologic flaws, indirect or imprecise), or very strong evidence of some other research design. Further research (if performed) is likely to have an impact on our confidence in the estimate of benefit and risk and may change the estimate.	Weak recommendation, alternative approaches likely to be better for some patients under some circumstances.

Literature search

The following PICOS strategy was defined: Population or disease: Humans; Intervention: nutrition; Comparator: nothing; Outcome: cognitive function; Study design: systematic reviews or meta-analysis.

A comprehensive literature review was performed using the Medline (via Ovid) database. The search was limited to published systematic reviews and meta-analyses and only those published in English were eligible. The search strategy combined keywords and Medical Subject Heading (MeSH) terms concerning the population (e.g. humans, men and women), the outcomes (e.g. cognitive impairment, cognitive decline, Alzheimer disease), the intervention (e.g. nutrition, diet, eating habits) and the type of study (e.g. systematic review, meta-analysis) by using Boolean indicators. Only studies published in the last ten years were eligible.

Data extraction and analysis

The GRADE (Grades of Recommendation, Assessment, Development, and Evaluation) approach classifies quality of the existing evidence available in systematic reviews and meta-analysis. Evidence was graded according to the classification of the American Academy of Sleep Medicine (AASM) and adapted from the Oxford Centre for Evidence-based Medicine Levels of Evidence, as presented in Table 1 (11).

Based on the GRADE process, a consensus statement was proposed for the best nutritional habits to prevent or to treat cognitive impairment.

Results

Based on the literature, the GRADE process led us to formulate seven key nutritional recommendations (Table 2). The first is global and concerns dietary pattern/habits while the fifth recommendation is a specific diet. The other recommendations focus on specific nutrients. However, based on lack of evidence, any other recommendation about the effect of other nutrients on cognition couldn't be realized. Our seven recommendations are developed below.

1) We recommend adherence to a Mediterranean diet to decrease the risk of cognitive decline: GRADE 1B

A Mediterranean diet is characterized by high intake of vegetables, fruits and nuts, cereals, fish and monounsaturated fatty acids (MUFA); relatively low intakes of meat and dairy products; and moderate

Table 2. Summary of Grading and recommendations for the preferred diet to prevent or to treat cognitive impairment

6 key nutritional recommendation	Key evidence literature	GRADE
Adherence to a Mediterranean diet	(7-9, 12, 13)	1B
High level of consumption of mono- and polyunsaturated fatty acids and a low consumption of saturated fatty acids	(8, 12, 14, 15)	1B
To increase fruit and vegetable intake	(8, 16, 17)	1B
A greater consumption of vitamin D	(18-21)	1C
Adherence to a ketogenic diet	(22, 23)	2C
Lower consumption of milk or dairy products	(8, 25)	2C
Caloric restriction	(26-29)	2C

consumption of alcohol.

This first recommendation is based on five recent systematic reviews published between 2011 and 2019 (7-9, 12, 13). Yusufov et al. (2017) found that 50/64 studies revealed an association between diet and Alzheimer disease (AD) incidence (7). More specifically, there was a 34% to 60.7% reduction in odds of AD with increase in adherence to a Mediterranean diet (7). These results are in line with those of Samadi et al. (2019) showing that 12/26 studies reported that Mediterranean diet was associated with the decrease of AD risk. The review of Aridi et al. (2017) also corroborates these results, showing that Mediterranean diet could protect against cognitive decline and decrease the risk of AD (10). Then, Otaegui-Arrazola et al. (2013) highlighted that 5/6 studies report an association between higher adherence to Mediterranean diet and decreased AD risk. Interestingly, in 2/3 studies, the risk of MCI and MCI conversion to AD was found to be lower in subjects with better adherence to this dietary pattern. In this review, Mediterranean diet has been demonstrated to improve cognitive functions (12). Finally, as reported by Solfrizzi et al. (2011), a high adherence to Mediterranean diet in AD patients could slow cognitive decline, reduced risk of progression from Mild Cognitive impairment (MCI) to AD, reduced risk of AD and decreased all-cause mortality (8).

In conclusion, these reviews join to say that adherence to a Mediterranean diet may help to decrease the incidence of AD.

2) We recommend a high level of consumption of mono- and polyunsaturated fatty acids and a low consumption of saturated fatty acids, to reduce the risk of cognitive decline: GRADE 1B

Fish and fish oil are rich sources of omega-3 fatty acids (i.e. monounsaturated fatty acids), specifically eicosa-pentaenoic acid (EPA) and docosa-hexaenoic acid (DHA). Alpha-linolenic acid (ALA) is an omega-3 fatty acid present in seeds and oils, green leafy vegetables, and nuts and beans. Linoleic acid (LA), an omega-6 fatty acid (i.e. polyunsaturated fatty acids), is present in grains, meats, and the seeds of most plants. Saturated fats are present in large quantities in meat, processed meat, milk, yogurt, cheese, butter are predominantly palmitic acid, predominantly in the form of palmitic acid.

This recommendation is based on four systematic reviews, including two meta-analysis, published between 2011 and 2019 (8, 12, 14, 15). The meta-analysis conducted on nine studies by Cao et al. (2019) highlighted that the highest category of saturated fat intake was associated with an increased risk of cognitive impairment (RR = 1.40; 95% CI: 1.02-1.91) and AD (RR: 1.87, 95% CI: 1.09-3.20) (14). However, the total and unsaturated fat intake was not statistically significantly associated with cognitive outcomes (15). The study of Solfrizzi et al. published in 2001 showed that elevated dietary monounsaturated fatty acids and n-3 polyunsaturated fatty acids and high fish consumption may have a beneficial effect on the risk of dementia (8). In 2013, Otaegui-Arrazola et al. have performed a systematic review concluding that the consumption of n-3 polyunsaturated fatty acids from diet has been associated with a decreased risk of AD and MCI, and better cognitive aging (12). In addition, high levels of n-3 polyunsaturated fatty acids biomarkers are related to better cognitive functions and higher brain volumes (12).

In conclusion, these four systematic reviews indicates that high-level of consumption of mono- and poly-unsaturated fatty acids and a low consumption of saturated fatty acids could reduce the risk of cognitive decline.

3) We recommend to increase fruit and vegetable intake: GRADE 1B

Fruits and vegetables contain a significant amount of vitamins and minerals, dietary fiber and beneficial non-nutrient substances such as plant sterols, flavonoids and other antioxidants. A large and varied consumption of fruits and vegetables makes it possible to cover the adequate intake of many of these essential nutrients.

This recommendation is based on three systematic reviews, including one meta-analysis, published between 2011 and 2019 (8, 16, 17). First, the meta-analysis of Mottaghi (2018), including six studies showed that increased fruit and vegetable intake was associated with

reduced risk of CI (OR: 0.79; 95% CI: 0.67-0.93; P=0.006) (16). Second, Solfrizzi et al. (2011) concluded that fruit and vegetable consumption is a protective factor for cognitive decline, dementia and AD, despite limited evidence. (8). Third, in the Science project, the authors highlighted that subjects included in the "high veggy" dietary pattern (based on eight nutritional items assessed with a food frequency questionnaire) had a higher MMSE scores (β 0.30 (0.21–0.64)). They concluded that better adherence to a "high veggy" dietary pattern was related to better global cognition (17).

In conclusion, despite the limited epidemiological evidence available, the literature seems to support the positive effect of fruit and vegetable high intake to prevent or treat cognitive impairment.

4) We recommend a greater consumption of vitamin D: GRADE 1C

Vitamin D plays an important role in the regulation of calcium absorption and homeostasis. The major source of vitamin D comes from the natural sun exposure. In addition, the main sources of dietary vitamin D are fish/fish products followed by eggs, fats/oils, bread/bakery products, and milk/dairy product.

The fourth recommendation is based on four recent systematic reviews published between 2015 and 2018 (18-21). Among these papers, three meta-analysis were performed. First, a meta-analysis highlighted severe vitamin D deficiency increased the risk of dementia (<25 nmol/L or 7-28 nmol/L) compared to people with sufficient vitamin D supply (≥50 nmol/L or 54-159 nmol/L) (point estimate 1.54; 95% CI 1.19-1.99, I2=20%) (19). Second, in the meta-analysis published by Goodwill and Szoeke (2017), low vitamin D was associated with worse cognitive performance (OR = 1.24, CI = 1.14-1.35) and cognitive decline (OR = 1.26, CI = 1.09-1.23); with a more marked effect in cross-sectional studies than in longitudinal studies. However, no significant difference between vitamin D supplementation and control on cognition was shown (SMD = 0.21, CI = -0.05 to 0.46) (20). Meta-analyses from Krause et al. (2015) have shown that low levels of vitamin D were associated with diminished cognitive function although the available evidence is not sufficient to establish causality (18). However, according to Butler et al. (2018), evidence about effects vitamin D plus calcium supplements was either insufficient, suggesting that these supplements did not reduce risk for cognitive decline (21).

In conclusion, the current literature suggest that low vitamin D levels might contribute to the development of dementia. Observational evidence demonstrates low vitamin D is related to poorer cognition. However, interventional studies still need to show a clear benefit from vitamin D supplementation.

5) We recommend that people who are interested can try a ketogenic diet, but that evidence does not yet support widespread uptake: GRADE 2C

The ketogenic diet is a low-carbohydrate (usually <50 g/day) and fat-rich diet that causes the body to break down fat into molecules called ketones. Ketones circulate in the blood and become the main source of energy for many cells in the body.

This recommendation is based on two recent systematic reviews (22, 23). The results of the review performed by Włodarek (2019) indicate that studies with human participants have demonstrated a reduction of AD symptoms after application of a ketogenic diet (22). These results corroborate those of White et al. (2017) (23). In this systematic review including four studies assessing the role of ketone supplementation in patients with either mild cognitive impairment (MCI) or Alzheimer's disease, the authors state that ketosis may be beneficial for subjects with AD (23). Finally, Lilamand et al. (2020) have recently conducted a systematic review assessing the effects of Ketogenic diet on cognition (24). Eleven human studies were included in this review and most of these studies showed that ketone supplementation or Ketogenic diet led to an improvement of cognitive outcomes (such as global cognition, memory and executive functions) (24).

In conclusion, the results suggesting the positive short-term effects of Ketogenic diet seems promising. However, neither data on the long-term application of the ketogenic diet in patients with neurodegenerative disease or data on its effects on disease symptoms are available.

6) We suggest a lower consumption of full-fat dairy and/or dairy fats, but that evidence does not yet support widespread uptake: GRADE 2C

In addition to milk, dairy products include yogurt, cheese, etc. This food category is rich in calcium, protein, potassium and phosphorus.

This recommendation is based on two systematic reviews published in 2011 and 2018 (8, 25) and is in line with the Mediterranean diet. In the systematic of Solfrizzi et al., only one out of the five principal prospective reports found a beneficial effect from dairy consumption in regard to cognitive function or MCI/dementia risk. Poorer cognitive function and an increased risk of vascular dementia were found to be associated with a lower consumption of milk or dairy products. On the other hand, three longitudinal studies found adverse effects on cognitive function from dairy fat. Indeed, consumption of whole-fat dairy products may be associated with cognitive decline in the elderly (8). In addition, Lee et al. performed a meta-analysis of three cohort studies and showed no significant association

between milk intake and cognitive decline outcome (pooled adjusted risk ratio = 1.21; 95% CI: 0.81, 1.82; the highest vs. the lowest intake) with large statistical heterogeneity (I 2 = 64.1%) (25).

In conclusion, the overall strength of evidence is inadequate for the positive effects of milk or dairy consumption on cognitive decline and disorders while whole-fat dairy products may be associated with late-life cognitive decline.

7) We suggest a caloric restriction, but that evidence does not yet support widespread uptake: GRADE 2C

Caloric restriction could be defined as a reduction in energy intake below the usual calorie consumption (≥10% in human studies and usually 20% or higher in rodent species).

The association between weight loss and cognitive function in older adults is still unclear. Siervo et al. (2011) estimated the effectiveness of intentional weight loss on cognitive function in overweight and obese adults (n=12: seven RCTs & five studies included a control group). The authors concluded that the effect of weight loss on memory (effect size 0.13, 95% CI 0.00-0.26, P=0.04) and on attention/executive functioning (effect size 0.14, 95% CI 0.01-0.27, P<0.001) is small, but significant. Weight loss appears to be associated with low-order improvements in executive/attention functioning and memory in obese, but not in overweight individuals (26).

The review of Gillette-Guyonnet, S. and B. Vellas (2008) corroborates this systematic review, suggesting that caloric restriction could be used to promote successful brain aging (27). In addition, according to Levenson and Rich (2007), caloric restriction has wide-ranging health benefits and may offer protection against age-related neuronal loss and neurodegenerative disorders such as Alzheimer's disease, possibly via enhanced adult neurogenesis (28).

More recently, Cremonini et al. (2019), stated that short periods of caloric restrictions are able to improve cognitive function (verbal memory) in elderly subjects but, according to these researchers, it is hard to believe that severe restrictions could be tolerated for long periods, especially in elderly subjects affected by neurodegenerative diseases (29).

In conclusion, despite the gaps in our current knowledge, the information we have seems to support the importance of caloric intake on the development and prevention of neurodegenerative disorders (28).

Insufficient evidence for three other nutrients are developed below

In addition to the previous recommendations, more studies are required in other components of dietary patterns in relation to cognition.

Protein

They are composed of one or more polypeptide chains. Each of these chains consists of amino acid residues linked together by peptide bonds. Protein can be represented as primary, secondary, tertiary, and quaternary structures. The primary sequence (amino acid) is the sequence of interest from a nutritional point of view.

Dietary protein and its amino acids influence cognition through its effects on risk factors related with cognitive decline. To date, according to the recent review of Glenn et al. (2019), there are limited scientific data directly linking protein/amino acid intake to cognitive decline (30). In this review, Glenn concluded that protein can help maximize physical activity results and physical activity is beneficial for maintaining cognitive status. However, a direct mechanism of action between protein and cognitive status remains unclear. Therefore, further investigations are necessary to understand the underlying mechanism explicating the effect of protein and its constituent amino acids on cognitive health. In 2015, Koh et al. had already performed a systematic review to obtain and appraise relevant studies on the effects of dietary protein or thiamine on cognitive function in healthy older adults (31). Seventeen eligible studies were included in this review and the authors concluded that evidence supporting an association between higher protein and/or thiamine intakes and better cognitive function was weak (31). Moreover, there was no evidence to support the role of specific protein food sources, such as types of meat, on cognitive function (31).

To date, the literature does not allow us to formulate recommendation on protein intake to prevent or manage cognitive decline.

Vitamins B6, B12 and folates

B vitamins are a water-soluble vitamin that play an important role in cell metabolism.

In 2019, Ford and Almeida performed a meta-analysis to examine the efficacy of treatment with vitamin B12, vitamin B6, or folic acid (B9) in slowing cognitive decline among older adults with and without cognitive impairment (32). This meta-analysis of randomized controlled trials including patients with pre-existing cognitive impairment (CI; n=10) or without cognitive impairment (NCI; n=21) found that B-vitamin supplementation does not improve cognitive status (Mini-Mental State Examination scores; CI studies: mean difference 0.16 (95% confidence interval -0.18 to 0.51) vs. NCI studies: mean difference 0.04 (95% confidence interval -0.10 to 0.18)) compared to placebo (32). The results of Ford and Almeida are consistent with those of

Forbes et al. published in 2015 (33). In the latest meta-analysis, including seven trials investigating the effects of various combinations of folate, B6 and/or B12 vitamins on cognitive performance, the authors showed no effect of vitamin B on MMSE score (three trials, mean difference 0.02, 95% CI 0.22 to 0.25) (33). In addition, the meta-analysis of Cao et al. (2015), conducted to determine whether there is an association between diet and risk of dementia, highlighted that vitamin B intake was related with decrease of dementia (RR: 0.72, 95 % CI: [0.54-0.96], P = 0.026) (14).

Because of the limitations of the available data, the lack of evidence of effect should not necessarily be interpreted as evidence of no effect. However, the current evidence does not allow us to establish a recommendation for vitamins B6, B9 (or folates) and B12 in the context of cognitive impairments.

Antioxidants

An antioxidant is a molecule that prevents or slows down oxidation by neutralizing free radicals. Excess free radicals are responsible for cell damage. Therefore, antioxidants delay or inhibit cellular damage.

Rafnsson et al. (2013) investigated, through a systematic review, the possible cognitive benefits of antioxidant nutrients in the elderly (34). According to the authors, the main supportive evidence came from two high quality studies. The first reported an accelerated decline in global cognition, attention, and psychomotor speed but also a decrease in plasma selenium levels over a 9 years period. The second study observed that people in the higher quartile of intake of vitamin C, E, and carotenes have less cognitive decline during the 3 years of follow-up. All associations persisted after adjustment for confounding factors. Although the evidence is limited in number, the authors concluded that antioxidants have potential protective effect against cognitive decline in older adults. Additional quality investigations are needed to confirm this possible association (34). In the meta-analysis of Forbes et al. (2015), three trials investigated the effect of vitamin E supplementation on cognitive impairment (33). Contrary to the conclusions of Rafsson et al. (34), no statistically significant effect on any of the cognitive outcomes examined was found (33). The conclusions of Crichton et al. (2013) also support those of Forbes. This review, assessing the association between antioxidant intakes (vitamins C, E, flavonoids, carotenoids) and cognitive function or risk for dementia included eight cross-sectional and thirteen longitudinal studies (35). The authors found mixed associations between antioxidant intake, cognition and risk of dementia and Alzheimer's disease (35).

These inconsistent results do not allow us to establish clear recommendations for antioxidants to prevent or manage cognitive impairments. Future studies are warranted to elucidate the effects of a high intake of dietary antioxidants on cognitive function.

Conclusion

Overall, some nutritional factors appear to either increase the risk of cognitive decline, or protect against it. Risk could be conferred by diets high in milk and dairy products. Of the dietary patterns that appear to offer some protection, the best evidence supports adherence to a Mediterranean diet to decrease the risk of cognitive decline. This evidence also contributes to support of a diet rich in mono- and poly- unsaturated fatty acids, fruit and vegetable, vitamin D and low in saturated fatty acids. Indeed, there is an overlap between the global recommendation related to dietary pattern (Mediterranean diet) and those related to specific nutrients (mono- and poly- unsaturated fatty acids, fruit and vegetable, vitamin D and low in saturated fatty acid). The current literature does not show enough to support more than a ketogenic diet as a promising, but unproved means of managing or preventing cognitive decline. Indeed, the results suggesting the positive short-term effects of Ketogenic diet seems promising. However, there is no evidence for long-term effects of the ketogenic diet among patients with neurodegenerative disease or for its effects on disease symptoms. In the same line, we suggest a lower consumption of whole-fat dairy products, while the existing evidence (mostly observational) is too poor to draw a firm conclusion about the beneficial effect of milk or dairy intake on the risk of cognitive impairments in adults. The literature also seems to support the importance of caloric intake on the development and prevention of neurodegenerative disorders, but that evidence does not yet support widespread uptake. Finally, more studies are required in other components of dietary patterns in relation to cognition, such as protein, vitamins B (B6, B12 and folates) or antioxidants.

Beside these recommendations, eating and drinking difficulties are recognized sources of ill health in people with dementia. A systematic review on importance of nutritional status in people with cognitive impairment or dementia showed: 1) a small positive short-term but unclear long term effects in controlled interventional studies; 2) a small evidence in food modification or dysphagia management studies and; 3) inconsistent evidence in eating assistance studies, whatever the settings, the level of care and support or the type and the degree of dementia (36). In addition, "finger foods" (foods that can be easily eaten with fingers) increase the pleasure of eating, the food consumption and the autonomy among frail older adults or those with dementia (37, 38). Pouyet et al. reported also that finger foods were frequently chosen and consumed by nursing home residents (39). It is also been concluded that finger food is an easy and cheap strategy (40).

In conclusion, it is clear that diet is an important

modifiable factor to prevent or protect against cognitive decline. However, more studies are required to determine the recommended duration and amounts of nutrients.

Ethical standard: ??????.

Conflict of interest: ??????.

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