

Nutrition has a Role in Dementia Risk Reduction and Management: Fact or Fiction?

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In recent years, clinical trials of potential disease-modifying therapeutics that target amyloid in people at risk of, or with, early Alzheimer's disease have yielded disappointing results. The continued absence of a 'cure' for dementia has contributed to delays in diagnosis and fuelled a belief among many primary and secondary healthcare professionals that nothing can be done for people with, or suspected of having, dementia. However, if one takes a broader view of the pathological processes involved in dementia – such as inflammation, mitochondrial dysfunction, synaptic loss and oxidative stress – there is increasing evidence that available interventions can decrease the risk and/or slow the progression of dementia. Interventions that combine a healthy approach to lifestyle with modifications to the nutritional components of diet have proved effective for optimising heart health and have now been shown to decrease the likelihood of dementia, regardless of genetic risk.

The Life's Simple 7 (LS7) score, which was originally proposed by the American Heart Association for maintaining cardiovascular health, has also been recommended for maintaining brain health. It comprises seven modifiable health factors, with higher scores associated with lower risk of dementia or cognitive decline: exercising regularly, eating healthily, not smoking, maintaining a healthy weight, keeping blood pressure in check, having healthy cholesterol levels, and

maintaining healthy blood sugar levels. Importantly, four of these factors relate to nutrition (eating healthily, maintaining a healthy weight, having healthy cholesterol levels, maintaining healthy blood sugar levels). Consequently, there has been increasing focus on the importance of nutrition, alone and in combination with lifestyle changes, as a protective factor for dementia, in terms of both modifying the risk of its development and slowing its progression. For example, the European Society for Clinical Nutrition and Metabolism (ESPEN) has published guidelines for nutritional care and support as an integral part of dementia management in all stages of the disease.

What evidence links dementia and nutrition?

Weight loss and associated nutritional deficits often begin prior to dementia diagnosis and become more common with disease progression. The causes of weight loss in people with dementia are complex and multifactorial, and the underlying mechanisms are not fully understood. It is known that changes in olfactory pathways occur many years before overt cognitive decline and this contributes to poor nutrition and weight loss. Studies have indicated the possible value of olfactory impairment as a potential pre-clinical marker of dementia, especially for *ApoE4* carriers. Adequate nutrition is vital for brain integrity and metabolism: certain dietary components are the main source of precursors of neurotransmitters, and processes that contribute to neurodegeneration in dementia (e.g. vascular damage, oxidative stress, inflammation) are modulated by specific nutrients. Marked deficiencies in certain vitamins (such as thiamine, folic acid, vitamin B12) are associated with cognitive impairment, and it is thought that milder deficiencies may exacerbate existing cognitive impairment in those at risk of, or with, dementia. Epidemiological studies provide evidence that specific dietary patterns may lower the risk of dementia, and, conversely, that poor dietary patterns are associated with increased dementia risk. Other potential factors that contribute to poor nutrition as dementia progresses include: difficulties with shopping for, storing and cooking food; forgetting to eat, and increasing inability to appreciate the value of a varied and adequate diet; and, in advanced dementia, difficulty with chewing and swallowing. In addition, non-dementia related factors, such as ageing, and other long-term conditions and associated medications, can have a negative effect on appetite and the ability to eat, and thereby contribute to poor nutrition.

Poor nutrition may initiate a cyclical process of deterioration in cognition that exacerbates cognitive impairment in those at risk of dementia and contributes to acceleration of the disease process in those who already have it. Poor nutrition is also associated with greater caregiver burden, which in turn may exacerbate nutritional issues. Therefore, identifying and addressing nutritional deficiencies has the potential to reduce cognitive impairment in those at risk of dementia, and the rate of decline in those who have the condition.

Are specific diets beneficial?

The Mediterranean and Dietary Approaches to Stop Hypertension (DASH) diets are similar in that they are both rich in fruit and vegetables, whole grains, beans, nuts, seeds and olive oil. Importantly, they also have a low content of meat and dairy products. The Mediterranean-DASH Intervention for Neurodegenerative Delay (MIND) diet combines the Mediterranean and DASH diets in a dietary pattern that focuses specifically on brain health. Studies have shown that the Mediterranean, DASH and MIND diets are associated with a significant 20–50% reduction in the risk of cognitive decline and dementia. Moreover, the Mediterranean and MIND diets have been associated with decreased plasma levels of inflammatory markers, the Mediterranean diet has been associated with improved endothelial function and lower adiposity, and the DASH diet has been associated with a reduced rate of cognitive decline, reduced risk of Alzheimer's disease, and larger total brain volumes in older adults. These results provide strong evidence that nutrition can have a positive impact on the risk of dementia and the rate of cognitive decline.

Are dietary supplements and vitamins beneficial?

Due to the roles played by vitamins, minerals and omega-3 fatty acids in the central nervous system and in maintaining brain health, nutritional supplementation has been suggested as a means of improving cognitive function and decreasing the risk of dementia. Studies of individual supplements have shown mixed results, and a 2018 Cochrane review concluded that there was no evidence to support single-agent vitamin or mineral supplementation in cognitively healthy adults in mid or late life as a meaningful strategy to decrease the risk of cognitive decline or dementia. More recently, two systematic reviews and meta-analyses concluded that folic acid

supplementation affords some protection against Alzheimer's disease, and that a combination of omega-3 polyunsaturated fatty acids and B vitamins in a multinutrient formula provides significant benefits on global cognition and episodic memory in older adults.

Are specific nutrient combinations beneficial?

A nutritional intervention called Souvenaid (formulated as a drink) was specifically designed to support synapse formation and reduce cognitive decline. It contains the active component, Fortasyn Connect, a multinutrient combination of specific fatty acids, vitamins and other key nutrients that are known to be decreased in patients with Alzheimer's disease. Evidence from a short-term study suggested a potential benefit in patients with early disease (mild cognitive impairment or prodromal Alzheimer's disease), and a long-term (8-year), placebo-controlled study showed trends for its benefit on the primary endpoint (change in a neuropsychological test battery score) at 24 months and significant benefits on secondary endpoints of function (clinical dementia rating-sum of boxes [CDR-SB]) and brain atrophy. A subsequent analysis at 36 months showed greater benefit with longer-term use on all previous endpoints, in comparison with placebo, and a more pronounced effect in people who were relatively early in the course of illness.

Summary

In 2015, the aforementioned ESPEN guidelines on nutrition in dementia reviewed available evidence for the role of nutrition in older people with dementia. The overall conclusion from the initiative was that '*Nutritional care and support should be an integral part of dementia management*'. The guidelines include recommendations on screening for malnutrition, monitoring of weight, and the importance of appropriate nutritional support during all stages of the disease. In those with more advanced dementia, they recommend that the individual's nutritional status be assessed in a comprehensive way, in order to develop personalised interventions that are nested in a multidisciplinary and integrated model of care. The guidelines do not advocate supplementation with single nutrients, unless there is a sign of deficiency.

Since 2015, considerably more evidence has emerged on the benefits of good nutrition for both people at risk of, and with, dementia. Nutritional components of diet

that were known to be effective for optimising heart health have now been shown to have a significant impact on brain health, decreasing the risk of dementia by 20–50%. The benefits of nutrition are not just seen for cognition and risk for dementia. Evidence from studies of specific diets (Mediterranean, DASH, MIND) has demonstrated benefit on broader aspects of neurodegeneration associated with dementia; namely, inflammation, mitochondrial dysfunction and oxidative stress. More recent evidence from the Finnish Geriatric Intervention Study to Prevent Cognitive Impairment and Disability (FINGER) study has shown the benefit of combining nutritional and life-style interventions.

The weight of evidence confirms the value of nutritional interventions alone, or in combination with other lifestyle approaches, in people at risk of, or with, dementia. The inclusion of these approaches in management of dementia should be embraced positively by healthcare professionals. These approaches have proven efficacy, no safety issues, are not costly and do not require adjustment of clinical practice or pathways to initiate. Rather, they need to be promoted for people at risk of, or with, dementia, just as similar approaches have been promoted for cardiovascular health.

FACT: There definitely is a role for nutrition in dementia risk reduction and management.

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