

Evidence to Decision Table

Problem Is the problem a priority?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<ul style="list-style-type: none"> ○ No ○ Probably no ○ Probably yes ● Yes ○ Varies ○ Don't know 	<p>Worldwide ageing of populations is strongly associated with dementia, causing major health, economic and social burdens. In 2015, it has been estimated that there were 50 million people with dementia in the world, and the number is predicted to double every 20 years, reaching 82 million in 2030 and 152 million in 2050.¹ Since no cure is available for Alzheimer’s disease, the main cause of dementia, prevention could be crucial in halting the rapid increase in the prevalence of this condition and international experts have called upon world-wide governments to make prevention of dementia one of their key health priorities.</p>	
Desirable Effects How substantial are the desirable anticipated effects?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<ul style="list-style-type: none"> ○ Trivial ○ Small ○ Moderate ○ Large ● Varies ○ Don't know 	<p>Different aspects of healthy nutrition are consistently reported to have beneficial association with cognitive performance in observational studies, but the evidence from trials is more inconsistent. It is important to consider that interventions with dietary modification that are able to improve several aspects of dietary intake are more likely to establish cognitive benefits as compared to supplementation with only some nutrients, although they are more demanding to execute. Dietary factors may have synergistic effects that are only evident in combinations of foods.⁹⁸</p> <p>The review of evidence presented here have identified 9 different interventions/comparisons:</p> <ol style="list-style-type: none"> 1. Supplement multi-complexes vs placebo in adults with normal cognition 2. Supplement multi-complexes vs placebo in adults with MCI 3. Poly Unsaturated Fatty Acids (PUFAs) vs placebo 4. Vitamin B vs placebo 5. Vitamin E vs placebo 6 Polyphenols vs placebo 7. Protein supplementation vs placebo 8. Chicken essence vs placebo 9. Mediterranean diet vs alternate or usual diet <p>For the outcomes of incident dementia and MCI, evidence was reported only for comparison 1 and 9 and neither supplementation with multi-complexes of vitamins and nutraceuticals, neither MeDi showed a direct effect in reducing the incidence of dementia and/or MCI.</p> <p>All the intervention/comparison included reported about cognitive outcomes. Polyphenols was the only category of supplement and nutraceuticals that was shown consistently to affect cognition beneficially, but evidence were deemed of low quality. Protein supplementations seems also to have</p>	

	<p>beneficial effect on cognition, in older adults, but the results are more inconsistent, and evidence were also deemed of low quality. There is evidence of moderate quality that MeDi can improve verbal and visual memory, almost significant results were obtained for global cognition (SMD 0.24; 95% CI-0.00 – 0.47) and a consistently positive, but not significant trend was reported for all the other cognitive outcomes (attention; working memory; processing speed; language; and executive function).</p> <p>In conclusion evidence of no effects was reported for multi complex, vitamin B and E, and PUFA supplementation, low quality evidence were reported of a beneficial effect of protein and polyphenols supplementation, and moderate evidence of a beneficial effect of MeDi was reported.</p>	
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Undesirable Effects
How substantial are the undesirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<ul style="list-style-type: none"> ○ Large ○ Moderate ○ Small ○ Trivial ● Varies ○ Don't know 	<p>Only one review considered here reported about adverse events.³⁹ Three multi-supplement complex interventions (DHA + EPA + vitamin E +soy phospholipids + tryptophan + melatonin; vitamin E + multivitamin; lyophilised royal jelly + ginkgo biloba + panax ginseng) were considered and none (N=860) showed an increased risk of any serious adverse event during the follow up period (moderate quality evidence).</p> <p>Overall dietary modification is safe and adverse events are rare, although they are more common in case of dietary supplementation interventions, especially of single nutrient, rather than intervention to promote healthy dietary patterns.</p> <p>Vitamin E and protein supplementation at high doses have been correlated to undesirable non-anticipated effects.</p>	

Certainty of evidence
What is the overall certainty of the evidence of effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<ul style="list-style-type: none"> ○ Very low ○ Low ● Moderate ○ High ○ No included studies 	<p>Evidence related to the efficacy of polyphenols and protein supplementation on cognition are of low quality. More certain (moderate quality) seems to be the beneficial effect of MeDi on some cognitive domains. It is important to notice that most of the trials are conducted in unselected populations in terms of nutrient status and focusing the supplement interventions on those with deficiencies in that specific nutrient may be a better strategy.</p> <p>No evidence is available of adverse effects of these interventions.</p> <p>In particular, the recommendation of not using supplements, if not needed for other reasons, should be emphasised.</p>	

Values		
Is there important uncertainty about or variability in how much people value the main outcomes?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<ul style="list-style-type: none"> ○ Important uncertainty or variability ○ Possibly important uncertainty or variability ○ Probably no important uncertainty or variability ● No important uncertainty or variability 	<p>Cognitive impairment and dementia can have a major impact in the life not only of the person affected but also of the close network of family and friends, as well as caregivers and health professional in general.^{99,100} Decreasing functional ability and dependency are the major components of this effect. Furthermore, dementia is the main cause of disability and institutionalization among older adults¹. Hence, reducing or delaying the risk/onset of dementia could result in lower costs for public healthcare services. Patients, caregivers, and policy makers are likely to be the people who will value these recommendations.</p>	
Balance of effects		
Does the balance between desirable and undesirable effects favour the intervention or the comparison?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<ul style="list-style-type: none"> ○ Favours the comparison ○ Probably favours the comparison ○ Does not favour either the intervention or the comparison ○ Probably favours the intervention ○ Favours the intervention ● Varies ○ Don't know 	<p>Evidence suggests that the desirable effects of the dietary interventions are larger than the undesirable effects. Low to moderate quality evidence suggests benefits of polyphenols, protein supplementation, and MeDi. Evidence on adverse events are not generally well reported but rare.</p> <p>MeDi probably favours the intervention</p> <p>Supplementation does not favour either intervention nor comparison.</p>	
Resources required		
How large are the resource requirements (costs)?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<ul style="list-style-type: none"> ○ Large costs ○ Moderate costs ○ Negligible costs and savings ○ Moderate savings ○ Large savings ● Varies ○ Don't know 	<p>In general interventions to establish healthy dietary patterns (like MeDi) are resource-intensive as they do require professional guidance and supervision. Group-based guidance and e-interventions are probably a way to reduce the costs. Intervention at a population level can also reduce costs.</p> <p>Supplemental interventions are cheaper and easier to execute.</p> <p>Healthy diets and supplements can be expensive in some countries.</p> <p>Dietary patterns may be hard to maintain, with increased costs in long term.</p>	<p>For more information: 'Best buys' and other recommended interventions to address non-communicable diseases (NCDs)</p> <p>http://apps.who.int/iris/bitstream/handle/10665/259232/WHO-NMH-NVI-17.9-eng.pdf?sequence=1</p>
Certainty of evidence of required resources		

What is the certainty of the evidence of resource requirements (costs)?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<ul style="list-style-type: none"> ○ Very low ○ Low ○ Moderate ○ High ● No included studies 	<p>No direct evidence available from the studies considered.</p>	
Cost effectiveness Does the cost-effectiveness of the intervention favor the intervention or the comparison?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<ul style="list-style-type: none"> ○ Favours the comparison ○ Probably favours the comparison ○ Does not favour either the intervention or the comparison ○ Probably favours the intervention ○ Favours the intervention ○ Varies ● No included studies 	<p>Although direct evidence was not identified in the present search, in general, dietary modification interventions (like MEDl) are resource-intensive and do require guidance and supervision but they are also the one more likely to have a beneficial effect⁹⁸. Group-based guidance and e-interventions are probably a way to reduce the costs. MeDi was shown to be cost-effective against degenerative pathologies.¹⁰¹</p> <p>On the other hand, supplemental interventions are cheaper and easier to execute but they are also less likely to have a wide variety of benefits in many outcomes (which is the case in dietary modification) so they are also less promising in terms of benefits.</p>	
Equity What would be the impact on health equity?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<ul style="list-style-type: none"> ○ Reduced ○ Probably reduced ○ Probably no impact ○ Probably increased ● Increased ○ Varies ○ Don't know 	<p>Lower socioeconomic groups are more likely to have earlier onset of dementia than higher socioeconomic groups. Older people from lower socioeconomic backgrounds are also more likely to experience cognitive dysfunction at earlier stages of cognitive decline and cognitive impairment, and will have fewer resources to cope with the symptoms than their counterparts from higher socioeconomic groups</p> <p>People from lower socioeconomic groups are more likely to live, work and age in physical and economic environments that do not support social connectedness, physical activity or mental stimulation. this can increase the risk of cognitive impairment and dementia in later life.¹⁰²</p> <p>Based on this it is believed that interventions to reduce risk of cognitive decline and dementia will increase equity in health.</p>	

	Furthermore, women are disproportionately affected with AD. The larger proportion of older women who have AD and other dementias is explained primarily by the fact that women live longer, on average, than men. ¹⁰³	
Acceptability Is the intervention acceptable to key stakeholders?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<input type="radio"/> No <input type="radio"/> Probably no <input type="radio"/> Probably yes <input checked="" type="radio"/> Yes <input type="radio"/> Varies <input type="radio"/> Don't know	Dietary interventions (especially the ones aimed at modified overall dietary patterns) have consistent benefits on cognition and other health parameters ⁹⁸ . Unhealthy diets and low physical activity contribute to many chronic diseases and disability; they are responsible for some 2 in 5 deaths worldwide and for about 30% of the global disease burden. ¹⁰⁴	
Feasibility Is the intervention feasible to implement?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<input type="radio"/> No <input type="radio"/> Probably no <input checked="" type="radio"/> Probably yes <input type="radio"/> Yes <input type="radio"/> Varies <input type="radio"/> Don't know	Costs and need of qualified staff have been identified as the key barriers; motivation will depend on the good planning of the intervention.	