Supplementary Material

Table 1: Ovid MEDLINE search terms

"Diet, Mediterranean**" OR "**diet" **OR** "diet*" **OR "**dietary Patterns" **OR** "dietary" **OR "**food" **OR** "unsaturated fats" **OR** "dietary fats" **OR** "fish oils" **OR** "olive oil" **OR "**fruit" **OR "**vegetables" **OR** "food habits" **OR** "eating habits" **OR** "dietary intervention" **OR** "food patterns" **OR** "dietary index" **OR** "diet supplementation" **OR "**dietary supplements**" OR** "nutritional supplements" **OR** "exercise" **OR** "walking" **OR** "physical fitness" **OR** "physical exertion" **OR** "Physical activity" **OR** "physical exercise*" **OR** "exercise therapy" **OR** "muscle strength" **OR** "exercise" **OR** "fitness" **OR** "aerobic" **OR** "strength" **OR** "exercise intervention" **OR** "cognitive rehabilitation" **OR** "cognitive stimulation" **OR** "cognitive training" **OR** "cognitive support" **OR** "memory function" **OR** "memory rehabilitation" **OR** "memory training" **OR** "memory stimulation" **OR** "memory aid" **OR** "memory support" **OR** "memory strategy" **OR** "memory management"
AND "cognition" **OR** "cognition disorders" **OR** "dementia" **OR** "memory" **OR** "vascular diseases" **OR** "cognition prevention" **OR** "Alzheimer's disease" **OR** "mild cognitive impairment" **OR** "brain" **OR** "neurophysiological tests" **OR** "MCI" **OR** "aMCI" **OR** "CIND" **OR** "non-aMCI" **OR** "Alzheimer*" **OR** "aging" **OR** "aged" **OR** "older adults" **OR** "seniors" **OR** "retirement" **OR** "retire*" **OR** "cognitive performance" **OR** "memory performance" **OR** "neuro*"
AND "health behaviour" **OR** "health behavior" **OR** "lifestyle" **OR** "lifestyle intervention" **OR** "behaviour change" **OR** "behavior change" **OR** "health promotion" **OR** "health improvement" **OR** "non-pharmacological" **OR** "program development" **OR** "program* development" **OR** "multidomain" **OR** "multicomponent" **OR** "health education"

Table 2: Summary of additional cognitive function measures used by studies

Measure	Study	Intervention	Cognitive function measure	Intervention Group and Control Group Results	Between Group Difference
Individual Cognitive Tests	Desideri et al., 2012[34]	990 mg HF vs IF *vs* LF cocoa flavanols per day	MMSE	HF(mean change +0.64 seconds*), IF (mean change +0.76 seconds*), LF (mean change +0.33 seconds*) (SDs not provided)	-
	Petersen et al., 2005[31]	2000 IU vit E, 10 mg donepezil or placebo	MMSE	Intervention (6 months Z score -0.53, SD ±2.28 – 36 months Z score -2.20, SD ±3.64); Control (6 months Z score -0.36, SD ±2.02 - 36 months Z score -2.75, SD ±4.04)	-
			ADAS-Cog	Intervention (6 months Z score –0.16, SD ±4.19 (original) / -0.47 SD ± 5.06 (modified) – 36 months Z score 4.59, SD ±6.54 (original) / 3.98, SD ± 7.56 (modified)); Control (6 months Z score -0.13, SD±3.34 (original) / -0.09, SD ±4.38 (modified) – 36 months Z score 3.74, SD ±6.97 (original) / 3.72, SD±8.54 (modified))	-
			CDR sum of boxes	Intervention (6 months Z score 0.17, SD ± 0.70 – 36 months Z score 1.67, SD ±2.18); Control (6 months Z score 0.14, SD ±0.86 – 36 months Z score 1.64; SD±2.55)	-
	Bo et al., 2017[28]	480mg of DHA + 720mg of EPA daily *vs* placebo	Mental arithmetic efficiency	Intervention mean difference 2.09 (SD±4.68); Control mean difference 0.33 (SD ±3.58)	-
			Space imagery efficiency	Intervention mean difference 2.45 (SD ±2.72); Control mean difference 0.00 (SD ±3.22)	✓
	Zhang et al., 2017[30]	2mg/day DHA *vs* placebo	Comprehension	Intervention mean score (baseline 11.97 (SD±1.23)-12 months 12.48 (SD±2.37)); Control mean score (baseline 13.42 (SD±1.43)-12 months 13.45 (SD±2.60))	-
			Vocabulary	Intervention mean score (baseline 10.24 (SD±2.44)-12 months 11.00 (SD±2.31)); Control mean score (Baseline 11.37 (SD±2.31)-12 months 11.35 (SD±2.04))	-
			Arithmetic	Intervention mean score (Baseline 11.37 (SD±3.09)-12 months 11.356 (SD±3.12)); Control mean score (Baseline 10.49 (SD±1.44)-12 months 10.36 (SD±3.54))	-
			Similarities	Intervention mean score (Baseline 11.82 (SD±2.31)-12 months 11.53 (SD±2.36)); Control mean score (Baseline 12.29 (SD±1.07)-12 months 12.35(SD±3.31)	-
			Picture completion	Intervention mean score (Baseline 11.35 (SD±2.45)-12 months 12.55 (SD±5.45)); Control mean score (Baseline 11.67 (SD±1.32)-12 months 11.29 (SD±3.56))	-
			Picture arrangement	Intervention mean score (Baseline 10.34 (SD±2.41)-12 months 10.69 (SD±2.83)); Control mean score (Baseline 11.71 (SD±2.67)-12 months 11.58 (SD±2.62))	-
			Object assembly	Intervention mean score (Baseline 10.26 (SD±2.73)-12 months 10.69 (SD±2.68)); Control mean score (Baseline 11.51 (SD±2.37)-12 months 10.67 (SD±2.54))	-

HF, High Flavonols; IF, Intermediate Flavonols; LF, Low Flavonols; MMSE, Mini Mental State Examination; SD, Standard Deviation; ADAS-Cog, Alzheimer's Disease Assessment Scale-Cognitive; CDR, Clinical Dementia Rating; GI, Glycaemic Index; tHcy, Total Homocysteine; CSF, Cerebrospinal Fluid; aMCI, amnesic Mild Cognitive Impairment; SEM, Standard Error of the Mean; P-tau, Phosphorylated-tau; CrPic, Chromium Picolinate; fMRI, Functional Magnetic Resonance; *Statistically significant difference ($p \leq 0.05$) within group; **Statistically significant difference ($p \leq 0.001$) within group; ✓Statistically significant difference ($p \leq 0.05$) between intervention & control group at intervention completion; - No statistically significant difference between intervention & control group at intervention completion; † Statistically significant difference between intervention & control at stated time-point

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			Digit symbol	Intervention mean score (baseline 13.27 (SD±3.31) – 12 months 14.11 (SD±2.32)); Control mean score (baseline 14.46 (SD±2.54) – 12 months 13.26 (SD±2.77))	✓
	Soininen et al., 2017[33]	Souvenaid, a 125ml once-a-day drink *vs* control	CDR-SB	Intervention mean change at 24 months (0.56, SD 1.32); Control mean change at 24 months (1.12, SD 1.72)	-
			NTB Z score	Intervention mean change at 24 months (-0.028, SD 0.453); Control mean change at 24 months (-0.108, SD 0.528)	-
	Philips et al., 2015[29]	625mg EPA+600mg DHA *vs* placebo	MMSE WB	Intervention mean score (month 1 26.6 (SD1.81) – month 4 26.9 (SD1.84)); Control mean score (month 1 26.0 (SD2.09) – month 4 26.4 (SD 2.08))	-
			MMSE S7	Intervention mean score (month 1 26.0 (SD 2.24) – month 4 25.8 (SD 1.86)); Control mean score (month 1 25.58 (SD2.55) – month 4 25.7 (SD 2.64))	-
			Word finding	Intervention mean score (month 1 11.58 (SD 2.19) – month 4 12.7 (SD 2.67); Control mean score (month 1 11.5 (SD 2.60) – month 4 11.9 (SD1.95))	-
Psycho-motor / motor Speed	Horie et al., 2016[37]	Nutritional counselling & calorie restriction *vs* standard care	Trail Making Test, part A	Intervention (mean change -6.1, 95% CI -22.6+-10.4); Control (mean change -0.7, 95% CI -17.3+-15.9)	-
	Bayer-Carter et al., 2011[38]	High fat/high GI diet *vs* Low fat/ low GI diet	Trail making test part A Stroop test	*No diet related changes in either group (high fat vs low fat diet) for motor speed. The authors did not, however, include these data in their published paper, merely stating this in the text.*	-
	Lee et al., 2013[27]	Fish oil supplementation with concentrated DHA+EPA *vs* placebo	Psychomotor Speed (digit symbol substitution)	Intervention (baseline mean score 5.5, 95% CI 3.72–7.22 – 12 months mean score 5.5, 95% CI 3.72-7.22); Control (baseline mean score 4.9, 95% CI 3.25–6.63 – 12 months mean score 4.9, 95% CI 3.25–6.63).	-
			Psychomotor Speed Z score	Intervention (mean change 0.19 (SD 0.84)); Control (mean change 0.04 (SD 0.60))	-
	Bo et al., 2017[28]	480mg of DHA + 720mg of EPA daily *vs* placebo	Perceptual speed	Intervention mean difference 3.61 (SD ±3.69); Control mean difference 0.81(SD ±2.83)	✓

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Global Cognitive Function	Lee et al., 2013[27]	Fish oil supplementation with DHA+EPA *vs* placebo	Global Cognitive Function (MMSE)	Intervention (baseline mean score 26.4, 95% CI 25.1–27.7 – 12 months mean score 26.6, 95% CI 25.7–27.6); Control (baseline mean score 26.4, 95% CI 25.1–27.6 – 12 months mean score 26.5, 95% CI 25.6–27.4)	-
	Desideri et al., 2012[34]	990mg HF *vs* IF *vs* LF cocoa flavanols per day	Overall Cognitive Function Z score	HF (Z score +0.69 (SD±0.22)**), IF (Z score +0.40 (SD±0.14)**), LF (Z score -0.07 (SD±0.38))	✓
	Petersen et al., 2005[31]	2000 IU vit E, 10 mg donepezil or placebo	Overall composite cognitive Z score	Intervention (6 months Z score 0.10, SD ±0.81† – 36 months Z score -0.70, SD±1.21); Control (6 months Z score -0.12, SD ±0.80 – 36 months Z score -0.65, SD ±1.35)	-
	De Jager et al., 2012[25]	0.8mg folic acid, 0.5mg vitamin B12 and 20mg vitamin B6 *vs* placebo	Global cognition (MMSE)	Intervention: Low tHcy baseline mean score 28.3, SD ±1.8 – 2 year follow up mean score 27.8, SD ±2.4; High tHcy baseline mean score 28.2, SD ±1.8 – 2 years follow up mean score 27.9, SD ±2.1; Control: Low tHcy baseline mean score 28.1, SD±1.6 – 2 years follow up mean score 28.1, SD±1.9; High tHcy baseline mean score, SD± 1.2 – 2 years follow up mean score 27.2, SD ±2.5. Those who had high baseline concentrations of homocysteine and were treated with B vitamins, were 1.58 more likely to provide a correct answer on the MMSE test than those in the placebo group	- ✓

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Cognitive Biomarkers	Bayer-Carter et al., 2011[38]	High fat/high GI diet *vs* Low fat/ low GI diet	CSF Aβ42	aMCI low diet baseline mean 397.18pg/ml (SEM 48.57) – week 4 mean 519.43pg/ml (SEM 49.55); aMCI high diet baseline man 439.04pg/ml (SEM 46.5) – week 4 mean 445.63pg/ml (SEM 47.44); Healthy controls low diet baseline mean 506.49pg/ml (SEM 50.94) – week 4 mean 452.04pg/ml (SEM 51.96); Healthy controls high diet baseline mean 384.03pg/ml (SEM 48.57) – week 4 mean 476.75pg/ml (SEM 58.10)	✓
			CSF Aβ40	aMCI low diet baseline mean 9212.94pg/ml (SEM 1206.06) – week 4 mean 9316.99pg/ml (SEM 1416.41); aMCI high diet baseline mean 7659.42pg/ml (SEM 946.11) – week 4 mean 8473.04pg/ml (SEM 1111.12); Healthy controls low diet baseline mean 9116.13pg/ml (SEM 1289.33) – week 4 mean 1011.44pg/ml (SEM 1514.20); Healthy controls high diet baseline mean 8796.32pg/ml (SEM 1289.33) – week 4 mean 9101.32pg/ml (SEM 1514.20)	-
			P- tau	aMCI low diet baseline mean score 88.80pg/ml (SEM 12.75) – week 4 mean 87.28pg/ml (SEM 10.78); aMCI high diet baseline mean 64.93pg/ml (SEM 11.18) – week 4 mean 66.10pg/ml (SEM 9.46); Healthy controls low diet baseline mean 61.67pg/ml (SEM 12.75) – week 4 mean 60.39pg/ml (SEM 10.78); Healthy controls high diet baseline mean 66.50pg/ml (SEM 14.25) – week 4 mean 65.68 pg/ml (SEM 12.05)	-
			Tau-protein	aMCI low diet baseline mean 113.18pg/ml (SEM 16.84) – week 4 mean 109.87 (SEM 13.86); aMCI high diet baseline mean 74.80pg/ml (SEM 15.38) – week 4 mean 75.76pg/ml (SEM 12.66); Healthy controls low diet baseline mean 80.41pg/ml (SEM 16.85) – week 4 mean 77.95pg/ml (SEM 13.86); Healthy controls high diet baseline mean 76.73pg/ml (SEM 18.83) – week 4 mean 73.47pg/ml (SEM15.50)	-
			Apolipo-protein E	aMCI low diet baseline mean 971.37ng/ml (SEM 100.37) – week 4 mean 1076.32ng/ml (SEM 109.83); aMCI high diet baseline mean 1115.34ng/ml (SEM 85.25) – week 4 mean 1076.32 (SEM 92.82); Healthy controls low diet baseline mean 1107.02ng/ml (SEM 100.87) – week 4 mean 1110.51ng/ml (SEM 109.83); Healthy controls high diet baseline mean 1161.80ng/ml (SEM 112.78) – week 4 mean 981.81ng/ml (SEM 122.79)	-

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Cognitive Markers	Krikorian et al., 2010c[32]	CrPic or placebo	fMRI scanning	CrPic group showed increased activation in the right thalamic, right temporal, right posterior parietal, and bilateral frontal regions in comparison to those in the placebo who showed no change	✓
	Zhang et al., 2017[30]	2mg/day DHA *vs* placebo	Left Hippocampus Vol (cm^3)	Intervention mean volume (baseline 2.61, SD±0.61 – 12 months 2.77, SD±0.40); Control mean volume (baseline 2.75, SD±0.36 – 12 months 2.74, SD±0.23)	✓
			Right Hippocampus Vol (cm^3)	Intervention mean volume (baseline 2.64, SD±0.53 – 12 months 2.69, SD±0.38); Control mean volume (baseline 2.65, SD±0.80 – 12 months 2.65, SD±0.37)	✓
			Total Hippocampus Vol (cm^3)	Intervention mean volume (baseline 5.25, SD±0.67 – 12 months 5.46, SD±0.40); Control mean volume (baseline 5.40, SD±0.39 – 12 months 5.39, SD±0.46)	✓
			Global Cerebral Vol (cm^3)	Intervention mean volume (baseline 991.77, SD±74.69 – 12 months 994.69, SD±79.67); Control mean volume (baseline 993.78, SD±54.16 – 12 months 994.98, SD±83.88)	✓
			Ventricular Vol (cm^3)	Intervention mean volume (baseline 5.90, SD±0.42 – 12 months 5.89, SD±0.28); Control mean volume (baseline 5.72, SD±0.72 – 12 months 5.65, SD±0.42)	-
	Soininen et al., 2017[33]	Souvenaid, a 125ml once-a-day drink *vs* control	Total Hippocampal Vol (cm^3)	Intervention mean change at 24 months (-0.30, SD 0.27); Control mean change at 24 months (-0.43, SD 0.33)	✓
			Whole brain Vol (cm^3)	Intervention mean change at 24 months (-20.27, SD 17.79); Control mean change at 24 months (-24.24, SD 20.93)	-
			Ventricular Vol (cm^3)	Intervention mean change at 24 months (5.96, SD 4.66); Control mean change at 24 months (7.80, SD 5.53)	✓
Adverse Events	Petersen et al., 2005[31]	2000 IU vit E, 10 mg donepezil or placebo	Adverse Events	Five participants died in the vitamin E group and five in the placebo	-
				Intervention group main adverse events: diarrhoea (10.2%) and cataract extraction (5.9%); Placebo group main adverse event: diarrhoea (6.6%)	-

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Table 3: Methodological quality of included studies as assessed by Jadad scale[22]

	Was the study described as randomised (includes use of words randomly, random and randomisation)? (Maximum = 2)	**Was the study described as double blind?** (Maximum = 2)	**Was there a description of withdrawals and dropouts?** (Maximum = 1)	**Total Score**
Krikorian et al., 2012[12]	1	0	0	1
Bayer-Carter et al., 2011[38]	1	0	0	1
Horie et al., 2016[37]	2	0	1	3
De Jager et al., 2012[25]	2	2	1	5
DeKosky et al., 2008[26]	2	2	1	5
Desideri et al., 2012[34]	2	2	1	5
Krikorian et al., 2010 [35]	1	1	0	2
Lee et al., 2013[27]	2	2	1	5
Petersen et al., 2005[31]	2	2	1	5
Krikorian et al., 2010 [36]	1	2	0	3
Krikorian et al., 2010 [32]	1	1	0	2
Ma et al., 2016[24]	2	1	1	4
Bo et al., 2017[28]	2	2	1	5
Zhang et al., 2017[30]	2	2	1	5
Soininen et al., 2017[33]	2	2	1	5
Phillips et al., 2015[29]	1	2	1	4

Table 4: Risk of bias score using the Cochrane classification (Higgins, 2011)[23]

	Selection Bias	Performance bias	Detection Bias	Attrition Bias	Reporting Bias
Krikorian et al., 2012[12]	Uncertain risk The authors stated "we randomly assigned 23 older adults" with no further details of allocation	High risk No details double-blinding of intervention between participants and researchers	High risk No details of any double blinding method used	Uncertain risk No details of withdrawals	Low risk All outcomes were reported in accordance with the methods section
Bayer-Carter et al., 2011[38]	Uncertain risk The authors stated "study participants were randomized" with no further details of allocation	Uncertain risk "Participants and all study personnel involved in data collection were masked to treatment assignment" – no further details	High risk No details of any double blinding method used	Uncertain risk No details of withdrawals	Low risk All outcomes were reported in accordance with the methods section
Horie et al., 2016[37]	Uncertain risk The authors state "this was a prospective, 1:1, randomized study" however no further details	Uncertain risk No details double-blinding of intervention between participants and researchers	Uncertain risk No details of any double-blinding method used	Low risk Withdrawals were accounted for. 5 participants lost to follow up – 3 in control group and 2 in intervention. Those who withdrew were not included in the final analysis.	Low risk All outcomes were reported in accordance with the methods section
De Jager et al., 2012[25]	Low risk "Centralized telephone randomization was used with full allocation concealment"	Low risk "Participants, study partners and those assessing outcomes were blind to the assignment of interventions"	Uncertain risk The study was double blinded with an intervention group and placebo however there is no detail if this was maintained or successful	Low risk Withdrawals were accounted for. 43 participants lost to follow up – 20 in placebo and 23 in intervention. Those who withdrew were not included in the final analysis	Low risk All outcomes were reported in accordance with the methods section

Table 4: Risk of bias score using the Cochrane classification (Higgins, 2011)[23]

	Selection Bias	Performance bias	Detection Bias	Attrition Bias	Reporting Bias
DeKosky et al., 2008[26]	Low risk "Assignment to G biloba or placebo was determined by permuted block design". "Randomization was done using a computer-generated, randomly permuted list"	Low risk "All clinical centre and coordinating centre personnel and participants were blinded to treatment assignment for the duration of the study"	Low risk This was a double-blinded study with an intervention group and placebo group however there is no detail if this was maintained or successful.	Uncertain risk Withdrawals were accounted for however the paper stated 195 participants were lost to follow up, however it is not clear how many had MCI.	Low risk All outcomes were reported in accordance with the methods section
Desideri et al., 2012[34]	Low risk "Computerized randomization of the products was conducted by an independent researcher".	Low risk "Neither the treating physicians, nor the patients were aware of treatment allocation"	Low risk This was a double blinded study were participants were unaware of treatment allocation	Low Risk There were no withdrawals from the study and all participants were included in the final analysis	Low risk All outcomes reported in accordance with methods section
Krikorian et al., 2010a[35]	Uncertain risk The authors indicate that "participants were randomly assigned" with no further details of allocation	Uncertain risk No details of double blinding of intervention between participants and researchers	Uncertain risk The authors state that the study was double blinded as participants received either an intervention or placebo drink, however there are no details if double blinding was successful or maintained	Uncertain risk All participants who were randomised were analysed in the results however there are no explicit details on withdrawals from the study	Low risk All outcomes were reported in accordance with the methods section
Lee et al., 2013[27]	Low risk "Randomisation was achieved using computer-generated random numbers in stratified permuted blocks of size four"	Uncertain risk The study was described as "double-blind" however no details of double blinding of intervention between participants and researchers	Uncertain risk The study was described as double blind however unclear if double blinding was maintained or successful	Low risk Withdrawals were accounted for a reasons described (1 participant in intervention group). All remaining participants were included in the analysis.	Low risk All outcomes reported in accordance with the methods section.

Table 4: Risk of bias score using the Cochrane classification (Higgins, 2011)[23]

	Selection Bias	Performance bias	Detection Bias	Attrition Bias	Reporting Bias
Petersen et al., 2005[31]	Low risk Participants were randomly assigned to treatment groups. "an adaptive allocation scheme for the treatment assignment"	Uncertain risk The study was described as "double-blind" but authors did not describe details of double blinding of intervention between participants and researchers	Uncertain risk The study was described as double blind however unclear if double blinding was maintained or successful	Uncertain risk "Primary analysis was conducted according to the intention-treat principle". Not clear how data from those who withdrew from the study was handled.	Low risk All outcomes reported in accordance with the methods section.
Krikorian et al., 2010b[36]	High risk The paper does not indicate that participants were randomly assigned. It followed the procedures of Krikorian et al., 2010a, however does not explicitly state randomisation procedures.	Low Risk Participants were blind to the supplement they received.	Uncertain risk The study was described as double blind however unclear if double blinding was maintained or successful	Uncertain risk Withdrawals were not accounted for or described.	Low risk All outcomes reported in accordance with the methods section
Krikorian et al., 2010c[32]	Uncertain risk Participants described as randomly assigned however no details of allocation	Uncertain risk The study was described as double-blind however no details given	Uncertain risk The study was described as double blind however it is not clear if this was maintained or successful	Uncertain risk Analysis included all participants who were randomised however it was no explicitly stated if there were any withdrawals	Low risk All outcomes were reported in accordance with the methods section

Table 4: Risk of bias score using the Cochrane classification (Higgins, 2011)[23]

	Selection Bias	Performance bias	Detection Bias	Attrition Bias	Reporting Bias
Ma et al., 2016[24]	Low risk "random cluster sampling"	Uncertain risk The study was described as double-blind however no details given	Low risk The authors stated that the study was double blinded as participants received either an intervention or placebo.	Low risk 21 withdrawals (10 in treatment, 11 in control) however all 90 participants who started the trails were included in ITT analysis	Low risk All outcomes were reported in accordance with the methods section
Bo et al., 2017[28]	Low risk "the randomization sequence was computer-generated by a blinded statistician"	Low risk Participants were blinded to the supplement they received	Uncertain risk The study was described as double blind however unclear if double blinding was maintained or successful	Low risk 22 drop-outs (n=12 in intervention group and n=10 in control). However, all 86 participants were included in ITT analysis	Low risk All outcomes were reported in accordance with the methods section
Zhang et al., 2017[30]	Low risk "random cluster sampling"	Low risk Participants were blinded to the supplement they received	Low risk Authors state that "all capsules were orange-flavoured and orange colour to protect the study blind"	Low risk 21 drop-outs (n=10 in intervention group and n=11 in control) however all 240 participants were included in ITT analysis	Low risk All outcomes were reported in accordance with the methods section
Soininen et al., 2017[33]	Low risk "Randomised 1:1 according to a randomisation list that was computer generated in block sizes of four"	Low risk Participants were blinded to the supplement they received	Low risk "The active and control products were isocaloric and similar in appearance and flavours. All study personnel and participants, were masked to treatment assignment"	Low risk 66 drop-outs (n=33 in intervention group and n=33 in control. However, all 311 participants were included in the ITT analysis	Low risk All outcomes were reported in accordance with the methods section

Table 4: Risk of bias score using the Cochrane classification (Higgins, 2011)[23]

	Selection Bias	Performance bias	Detection Bias	Attrition Bias	Reporting Bias
Phillips et al., 2015[29]	Uncertain Risk Authors indicate that this was a randomised controlled trial but no details of the randomisation process	Low risk Participants were blinded to the supplement they received	Low risk "Participants and their carers and the researchers conducting the cognitive assessments and the plasma fatty-acid assays were blind to the identity of the treatments"	Low risk "76 people (57 CIND and 19 AD) were recruited and there were no dropouts. However, four participants (2 CIND randomised to placebo and 2 AD, one randomised to omega-3 supplements and one to placebo) did not complete all visits."	Uncertain risk Some outcome measures mentioned in the methods section did not appear in the reported results

Most Frequently Used Cognitive Function Tests

Rey Auditory Verbal Learning Test (RAVLT) – this test evaluates short-term auditory-verbal memory, rate of learning, learning strategies, retention of information, and differences between learning and retrieval. Participants are given a list of 15 unrelated words repeated over five different trials and are asked to repeat. Another list of 15 unrelated words are given and the client must again repeat the original list of 15 words and then again after 30 minutes. Approximately 10 to 15 minutes is required for the procedure (not including 30 min. interval).

Digit span task (forward or backward) – this test is used to measure working memory's number storage capacity. Participants see or hear a sequence of numerical digits and are tasked to recall the sequence correctly, with increasingly longer sequences being tested in each trial. The participant's span is the longest number of sequential digits that can accurately be remembered. Digit-span tasks can be given forwards or backwards, meaning that once the sequence is presented, the participant is asked to either recall the sequence in normal or reverse order.

Trail making test, part A and B – this is a neuropsychological test of visual attention and task switching. It consists of two parts in which the subject is instructed to connect a set of 25 dots as quickly as possible while still maintaining accuracy. The test can provide information about visual search speed, scanning, speed of processing, mental flexibility, as well as executive functioning

Visual reproduction I and II – A subtest of the Wechsler Memory Scale (WMS). Tests of visual reproduction are used to assess immediate and delayed recall for a visual drawing task.

Digit symbol substitution - It is part of the Wechsler Adult Intelligence Scale. The DSST requires response speed, sustained attention, visual spatial skills. The DSST requires that the participant fill in a series of symbols correctly coded within 90 seconds. In this test the higher the score the better the person's performance.

Hopkins Verbal Learning Test–Revise (HVLT-R) - Assesses verbal learning and memory (immediate recall, delayed recall, delayed recognition). Consists of a 12-item word list, composed of four words from each of the three semantic categories. The subject is instructed to listen carefully as the examiner reads the word list and attempt to memorize the words. The word list is then read to the subject at the approximate rate of one word every 2 seconds. The patient's free recall of the list is recorded. The same procedure is repeated for two more trials. After the third learning trial, the patient is read 24 words and is asked to say "yes" after each word that appeared on the recall list (12 targets) and "no" after each word that did not (12 distractors). Half of the distractors are drawn from the same semantic categories as the targets (related distractors) and half are drawn from other categories (unrelated distractors).

The Consortium to Establish a Registry for Alzheimer's Disease (CERAD) – A comprehensive neuropsychological battery including Verbal Fluency, Boston Naming Test, Mini-mental State Exam, Word List Memory, Constructional Praxis, Word List Recall, Word List Recognition and Recall of Constructional Praxis.

Brief Visuospatial Memory Test - In three Learning Trials, the respondent views the stimulus page for 10 seconds and is asked to draw as many of the figures as possible in their correct location on a page in the response booklet. A Delayed Recall Trial is administered after a 25-minute delay. Last, a Recognition Trial, in which the respondent is asked to identify which of 12 figures were included among the original geometric figures, is administered.

Story recall - participants are asked to memorize more complex sentences rather than a simple list of words. Therefore, the SRT requires more attention, greater learning ability, and better language comprehension, and it provides a more specific examination of the encoding, storage, and retrieval

processes of the memory system, as well as the words or meaning of sentences that affect the memory system (Lezak, 1995)

Word list - a common feature of these tests is that several lists of words are used to assess verbal memory. The participants are asked to memorize the words several times and then to complete an immediate recall test, a 20- minute delayed recall test, and a recognition test (Lezak, 2004).

Verbal Paired Associates Test (V-PAL) - The Verbal Paired Associates subtest from the Wechsler Memory Scale-III (WMS-III) is one of the most widely used instruments for assessing explicit episodic memory performance.

Spatial Paired Associate Learning Task - assesses visual memory and new learning. Subjects learn and remember which of a number of objects goes in different spatial locations. On a given trial, two different objects are presented; one in its correct location; the other in an incorrect location.

California Verbal Learning Test - This procedure examines several aspects of verbal learning, organization, and memory.

Verbal Fluency -The verbal fluency test is a short test of verbal functioning. It typically consists of two tasks: category fluency (sometimes called semantic fluency) and letter fluency (sometimes called phonemic fluency). In the standard versions of the tasks, participants are given 1 min to produce as many unique words as possible within a semantic category (category fluency) or starting with a given letter (letter fluency). The participant's score in each task is the number of unique correct words

Clock Drawing Test (CDT) - the instructions are for the person to draw a clock and put the hands at a specific time that the doctor says (usually it is 11:10). Can be used to assess executive functioning, Global cognitive status, visuospatial abilities or attention. 1 point is given for drawing the clock and getting the time correct (indicating the absence of dementia) and 0 points are given if these two criteria are not met (indicating further evaluation is needed).

Modified Wisconsin Card Sorting Test (M-WCST) - The M-WCST is a modification of the original Wisconsin Card Sorting Test that eliminates all cards from the original 128-card deck that share more than one attribute with a stimulus card. The resulting 48-card deck is used along with four stimulus cards to assess perseveration and abstract reasoning with minimal client frustration.

Stroop colour word test - When the name of a colour (e.g., "blue", "green", or "red") is printed in a colour that is not denoted by the name (e.g., the word "red" printed in blue ink instead of red ink), naming the colour of the word takes longer and is more prone to errors than when the colour of the ink matches the name of the colour (Stroop, 1935)

CLOX – The Executive Clock Drawing Task.

Block design test – assesses spatial visualization ability and motor skill. The test-taker uses hand movements to rearrange blocks that have various colour patterns on different sides to match a pattern. The items in a block design test can be scored both by accuracy in matching the pattern and by speed in completing each item.

References

Strauss E, Sherman EMS, & Spreen O. (2006) A compendium of neuropsychological tests: administration, norms, and commentary, Third edn, Oxford University Press, Inc., New York; 4.
Lezak MD. (1995) Neuropsychological assessment (3rd ed.). New York, NY: Oxford University Press.
Lezak MD, Howieson DB, & Loring DW. (2004) Neuropsychological assessment (4th ed.). New York, NY: Oxford University Press.

Diagnostic Criteria for MCI

European Consortium on Alzheimer's Disease – *"MCI should correspond to cognitive complaints coming from the patients or their families; the reporting of a relative decline in cognitive functioning during the past year by a patient or informant; cognitive disorders as evidenced by clinical evaluation; absence of major repercussions on daily life; and absence of dementia".*

Portet F, Ousset PJ, Visser PJ, *et al.* (2006) Mild cognitive impairment (MCI) in medical practice: a critical review of the concept and new diagnostic procedure. Report of the MCI Working Group of the European Consortium on Alzheimer's disease. *J Neurol Neurosurg Psychiatry* **77**, 714–718.

Clinical Dementia Rating (CDR) – *"5-point scale used to characterize six domains of cognitive and functional performance applicable to Alzheimer disease and related dementias: Memory, Orientation, Judgment & Problem Solving, Community Affairs, Home & Hobbies, and Personal Care".*

0 = Normal

0.5 = Very Mild Dementia

1 = Mild Dementia

2 = Moderate Dementia

3 = Severe Dementia

Hughes CP, Berg L, Danziger WL, *et al.* (1982) A new clinical scale for the staging of dementia. Br J Psychiat 140, 566–572.

Petersen Criteria (1999) – "*The first clinical criteria for MCI focused primarily on episodic memory impairment. Deficits in non-memory cognitive domains (e.g., executive control, language or visuospatial abilities) were allowed, but deficits found solely in non-memory domains were not considered"*

Petersen RC, Smith GE, Waring SC, *et al.* (1999) Mild cognitive impairment: clinical characterization and outcome. Arch Neurol 56, 303-8.

Petersen criteria (2004) – "*revision of the 1999 criteria to include subtypes of MCI. Patients with MCI were classified as amnestic MCI if showed performance deficits on neuropsychological tests of episodic memory, or non-amnestic MCI if patients exhibited performance deficits on neuropsychological tests of non-memory domains of cognition. Impairment could be limited to one cognitive domain (MCI single domain) or to multiple domains (MCI multiple domains)".*

Petersen RC. (2004) Mild cognitive impairment as a diagnostic entity. J Intern Med 256, 183–194.

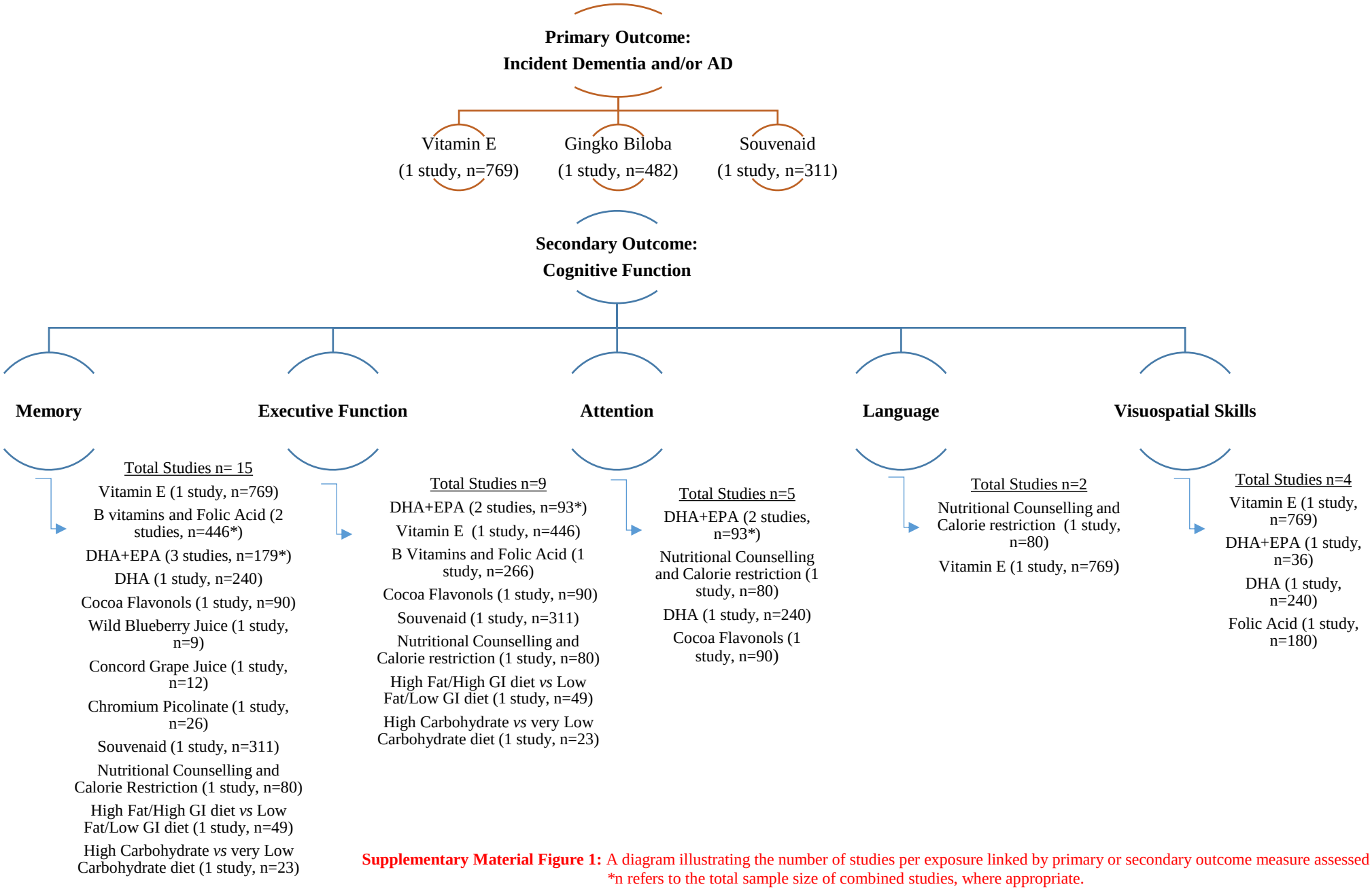
International working group on MCI guidelines (Winblad 2004) – *"the specific recommendations for the general MCI criteria include the following: (i) the person is neither normal nor demented; (ii) there is evidence of cognitive deterioration shown by either objectively measured decline over time and/or subjective report of decline by self and/or informant in conjunction with objective cognitive deficits; and (iii) activities of daily living are preserved and complex instrumental functions are either*

intact or minimally impaired. Like Petersen (2004), this criteria considered the differentiation of MCI into subtypes"

Winblad B, Palmer K, Kivipelto M, *et al*. (2004) Mild cognitive impairment: beyond controversies, towards a consensus: report of the International Working Group on Mild Cognitive Impairment. *J Intern Med*. 256, 240-246.

Dubois et al., (2007) (NINCDS-ADRDA criteria) – *"The symptomatic pre-dementia phase of Alzheimer's disease, generally included in the mild cognitive impairment category; this phase is characterised by symptoms not severe enough to meet currently accepted diagnostic criteria for AD. It must be distinguished within the broad and heterogeneous state of cognitive functioning that falls outside normal ageing. This state has been described by a wide range of terms including age-associated memory impairment, age-related cognitive decline, age-associated cognitive decline, mild cognitive disorder, mild neurocognitive disorder, cognitively impaired not demented, and mild cognitive impairment."*

Dubois B, Feldman HH, Jacova C, *et al*. (2007) Research criteria for the diagnosis of Alzheimer's disease: revising the NINCDS-ADRDA criteria. *Lancet Neurol* **6**, 734–46.



Supplementary Material Figure 1: A diagram illustrating the number of studies per exposure linked by primary or secondary outcome measure assessed
*n refers to the total sample size of combined studies, where appropriate.