Appendix 2 (as supplied by the authors): characteristics of included studies

Table S1

Study/Location	de Jager 2012; UK *Companion paper:* Smith 2010
Objective	To determine the effect of B vitamins on cognitive and clinical decline
Methods	Design: RCT Recruitment: recruited through advertisements in the local newspaper or radio seeking elderly people with concerns about their memory Inclusion Criteria: age ≥ 70 years; study partner available as informant, and diagnosis of amnestic or non-amnestic MCI according to Petersen's criteria Exclusion Criteria: diagnosis of dementia or being treated with anti-dementia drugs; active cancer; major stroke within past 3 months; treatment with methotrexate, anti-cancer or anti-epileptic drugs, or taking folic acid > 300 mg/d pyridoxine > 3 mg/d or vitamin B12 > 1.5 mg/d by mouth or any dose by injection
Participants	Sample: *n* = 271 Intervention *n* = 138; Control *n* = 133 Mean Age (SD): Intervention: 76.8 (5.1) years; Control: 76.7 (4.8) years Gender [Female n(%)]: Intervention: 70 (63.6); Control: 73 (64.6) Loss to Follow-up Intervention *n* = 23; Control *n* = 20
Intervention	Description of Intervention: daily dose of TrioBe Plus W, containing 0.8mg folic acid, 0.5mg cyanocobalamin and 20mg pyridoxine HCl Description of Control: placebo Duration of Intervention: 24 months Length of Follow-up: immediate post
Study/Location	Doody 2009; US
Objective	To investigate the effect of 48 weeks of donepezil treatment on amnestic MCI
Methods	Design: RCT Recruitment: not reported Inclusion Criteria: global Clinical Dementia Rating (CDR) score of 0.5 at screening with the Memory Box score of 0.5 or 1.0, with no more than 2 other box scores rated as high as 1.0, and no box score 1.0; Mini-Mental State Examination (MMSE) score 24 –28 inclusive (or 24 –30 before protocol amendment); Logical Memory II Delayed Paragraph Recall subtest of the Wechsler Memory Scale–Revised score 8 (16 or more years of education), 4 (8 –15 years of education), or 2 (0 –7 years of education); and Rosen modified Hachinski Ischemia scale score ; an informant; a CT scan or MRI study within 12 months of screening showing no clinical evidence of infection, infarction, other focal lesions, or clinically significant comorbid pathologies Exclusion Criteria: diagnosis of probable or possible vascular dementia; another form of dementia; a neurologic or psychiatric disorder; a sleep disorder that could affect cognitive performance; drug or alcohol abuse or dependence within the previous 5 years; uncontrolled hypertension regardless of antihypertensive medication; uncontrolled diabetes mellitus; any medical condition deemed incompatible with study participation; past treatment with a ChEI or memantine for 1 month or within 3 months of screening; anticholinergics, anticonvulsants, antiparkinsonian agents, stimulants, cholinergic agents, antipsychotics, or antidepressants or anxiolytics with anticholinergic or procholinergic effects
Participants	Sample: *n* = 821 Intervention *n* = 409; Control *n* = 412 Mean Age (SD): Intervention: 70.2 (9.71) years; Control: 69.8 (10.32) years Gender [Female (%)]: Intervention: 48.3%; Control: 42.6% Loss to Follow-up: Intervention: *n* = 165; Control: *n* = 114
Intervention	Description of Intervention: donepezil (5 mg/day for 6 weeks, 10 mg/day for 42 weeks) Description of Control: placebo Duration of Intervention: 48 weeks Length of Follow-up: immediate post
Study/Location	Feldman 2007; Canada
Objective	To assess the effect of rivastigmine in patients with MCI on the time to clinical diagnosis of Alzheimer's disease (AD) and the rate of cognitive decline
Methods	Design: RCT Recruitment: referral to the research centres, through advertising, or from patients known to the investigators at the participating research centres Inclusion Criteria: entry score of less than 13 on the 17-item Hamilton rating scale for depression (HAM-D) with HAM-D item 1 (depressed mood) of 1 or lower

Appendix to: Fitzpatrick-Lewis D, Warren R, Ali MU, Sherifali D, Raina P. Treatment for mild cognitive impairment: a systematic review and meta-analysis. *CMAJ Open* 2015. DOI:10.9778/cmajo.20150057.

	Exclusion Criteria: patients who met the AD diagnostic criteria of the Diagnostic and Statistical Manual of Mental Disorders IV or the AD criteria of the National Institute of Neurological and Communicative Disorders and Stroke-AD and Related Disorders Association; any primary neurodegenerative disease; any advanced, severe unstable medical condition that could interfere with assessment; uncontrolled seizure disorder; score of > 4 on the modified Hachinski ischemic scale; documented history of transient ischemic attack; any severe or unstable cardiovascular disease or asthmatic conditions; hypersensitivity to cholinesterase inhibitors; treatment with cholinergic drugs during 2 weeks before trial, or with rivastigmine during the previous 4 weeks; prior participation in a previous clinical study of rivastigmine
Participants	Sample: *n* = 1018 Intervention *n* = 508; Control *n* = 510 Mean Age (SD): Intervention: 70.3 (7.4) years; Control: 70.6 (7.6) years Gender [Female n(%)]: Intervention: 270 (53.1%); Control: 262 (51.4%) Loss to Follow-up: Intervention: 196; Control: 164
Intervention	Description of Intervention: rivastigmine (3–12 mg daily) Description of Control: placebo Duration of Intervention: up to 48 months Length of Follow-up: immediate post
Study/Location	Lee 2013; Malaysia
Objective	To investigate the effects of fish oil supplementation on cognitive function in elderly people with MCI
Methods	Design: RCT Recruitment: recruited from middle to low socioeconomic households in Cheras, Kuala Lumpur, Malaysia with help of the Housing Management Officer, and residential representatives, as well as using posters, banners, invitation letters, informational lectures and word-of-mouth invitation Inclusion Criteria: diagnosed with MCI residing in their own home; not currently living alone or on a waiting list for a nursing home. Exclusion Criteria: any type of newly diagnosed neurodegenerative disease, psychiatric disease or mental disorder; taking omega-3 preparations, vitamin supplements/drinks/injections with doses of vitamin B6, folate or vitamin B12, vitamin E and ginkgo biloba for the past year; suffering from alcohol abuse or from a concomitant disease, such as uncontrolled diabetes, cancer and kidney failure
Participants	Sample: *n* = 36 Intervention *n* = 18; Control *n* = 18 Mean Age (SD): Intervention: 66.4 (5.1) years; Control: 63.5 (3.0) years Gender [Female n(%)]: Intervention: 14 (82.4%); Control: 13 (72.2%) Loss to Follow-up Intervention *n* = 1; Control *n* = 0
Intervention	Description of Intervention: 3 1-g soft gelatine capsules each day, each containing 430 mg of DHA and 150 mg of EPA. The total dosage for the fish oil group was approximately 1.3 g DHA and 0.45 mg EPA daily Description of Control: placebo Duration of Intervention: 12 months Length of Follow-up: immediate post
Study/Location	Naeini 2014; Iran
Objective	To investigate the effect of Vitamins E and C on cognitive performance among the elderly in Iran
Methods	Design: RCT Recruitment: retiree clubs Inclusion Criteria: not reported Exclusion Criteria: obvious disabling disease; alcohol intake; smoking; routine consumption of neurologic or antioxidant drugs
Participants	Sample: *n* = 256 Intervention: *n* = 127; Control *n* = 129 Mean Age (SD): Intervention 66.5 (0.39) years; Control: 66.3 (0.38) years Gender [Female n(%)]: Intervention: 64 (50.4%); Control: 72 (55.8%) Loss to Follow-up: *n* = 40 overall
Intervention	Description of Intervention: 300 mg/d of vitamin E plus 400 mg/d vitamin C Description of Control: placebo Duration of Intervention: 12 months Length of Follow-up: immediate post
Study/Location	Petersen 2005; US; Canada *Companion papers:* Lu 2009
Objective	To determine if there is a benefit of using donepezil or vitamin E in patients with MCI

Methods	Design: RCT Recruitment: recruited from 69 Alzheimer's Disease Cooperative Study sites Inclusion Criteria: have amnestic MCI of a degenerative nature; impaired memory; a Logical Memory delayed-recall score approximately 1.5 to 2 SD below an education-adjusted norm; a Clinical Dementia Rating of 0.5; a score of 24 to 30 on the Mini–Mental State Examination; age 55–90 years
Participants	Sample: *n* = 769 Intervention 1 (Donepezil) *n* = 253; Intervention 2 (Vitamin E) *n* = 257; Control *n* = 259 Mean Age (SD): Intervention 1: 73.1 (7.1) years; Intervention 2:72.8 (7.3) years; Control: 72.9 (7.6) years Gender [Female n(%)]: Intervention 1: 112 (44%); Intervention 2: 119 (46%); Control: 121 (47%) Loss to Follow-up: not reported
Intervention	Description of Intervention: Intervention 1 (Donepezil, placebo Vitamin E and multivitamin): initial dose of 5 mg daily; increased to 10 mg daily after 6 weeks Intervention 2 (Vitamin E, placebo donepezil, multivitamin): initial dose of Vitamin E of 1000 IU daily; increased to 2000 IU daily after 6 weeks Description of Control: placebo donepezil, placebo vitamin E, and multivitamin Duration of Intervention: 36 months Length of Follow-up: immediate post
Study/Location	Rojas 2013; Argentina
Objective	To examine the efficacy of a 6-month cognitive intervention program in patients with MCI and to assess patients' condition at one year follow-up
Methods	Design: RCT Recruitment: referral pool of 120 community-dwelling patients who had consulted the memory clinic of a public general hospital between January 2002 and April 2008 Inclusion Criteria: all MCI subtypes Exclusion Criteria: other neurologic diseases or major psychiatric diagnoses consistent with the Diagnostic and Statistical Manual of Mental Disorders criteria; drug or alcohol abuse or dependence in the past 5 years; treatment with cholinesterase inhibitors (donepezil, rivastigmine, or galantamine) or memantine
Participants	Sample: *n* = 46 Intervention: *n* = 24; Control: *n* = 22 Mean Age (SD): Intervention: 72 (14.29) years; Control: 76.93 (7.05) years Gender [Female n(%)]: Intervention: 6 (25%); Control: 7 (32%) Loss to Follow-up: Intervention *n* = 9; Control *n* = 7
Intervention	Description of Intervention: multi-modal intervention program included cognitive stimulation training sessions and cognitive training delivered by 2 experienced neurophysiologists in 2 weekly group (4–5 participants) sessions of 120 minutes located in hospital-based outpatient memory clinics over 6 months Description of Control: no treatment Duration of Intervention: 6 months Length of Follow-up: 6 months
Study/Location	Suzuki 2012; Japan
Objective	To examine the effects of a multicomponent exercise program on the cognitive function of older adults with aMCI
Methods	Design: RCT Recruitment: volunteer databases Inclusion Criteria: community dwelling adults ≥ 65 years; Petersen criteria for MCI Exclusion Criteria: a CDR = 0, 1, 2, and 3; a history of neurologic, psychiatric, and cardiac disorders or other severe health issues; use of donepezil; loss of independence in basic activities of daily living (ADL); current participation in other research projects
Participants	Sample: *n* = 50 Intervention: *n* = 25; Control: *n* = 25 Mean Age (SD): Intervention: 75.3 (7.5) years; Control: 76.8 (6.8) years Gender [Female n(%)]: Intervention: 12 (48%); Control: 11(44%) Loss to Follow-up: Intervention: *n* = 1; Control *n* = 2
Intervention	Description of Intervention: multicomponent exercise group under the supervision of physiotherapists for 90 minute/d, 2 d/wk, for a total of 80 times over 12 months Description of Control: 3 education classes on health promotion (information on aging, healthy diet, oral care, brain image diagnosis, prevention of urinary incontinence, and health checks) Duration of Intervention: 12 months Length of Follow-up: immediate post
Study/Location	Suzuki 2013; Japan

Objective	To examine the effect of multicomponent exercise program on memory function in older adults with MCI
Methods	Design: RCT Recruitment: recruited from 2 volunteer databases; selected by random sampling or at medical check-up in Obu, Japan Inclusion Criteria: community-dwelling individuals aged ≥ 65 years; meet Petersen criteria for MCI; objective impairments in either episodic memory and/or executive functioning at least 1.5 standard deviations below the age-adjusted mean for at least one of the neuropsychological tests Exclusion Criteria: a CDR = 0, or a CDR of 1–3; a history of neurologic, psychiatric, or cardiac disorders or other severe health issues; use of donepezil; impairment in basic activities of daily living (ADL); participation in other research project
Participants	Sample: *n* = 100 Intervention: *n* = 50; Control: *n* = 50 Mean Age (SD): Intervention = 74.8 (7.4) years; Control = 75.8 (6.1) years Gender [Female n(%)]: Intervention *n* = 25 (50%); Control *n* = 24 (48%) Loss to Follow-up Intervention: *n* = 3; Control *n* = 5
Intervention	Description of Intervention: 6-month, multicomponent exercise program including biweekly 90-minute sessions involving aerobic exercise, muscle strength training, postural balance retraining, and dual-task training and focus on promoting exercise and behaviour change Description of Control: 2 education classes on health promotion: information regarding healthy diet, oral care, prevention of urinary incontinence, and health checks Duration of Intervention: 6 months Length of Follow-up immediate post
Study/Location	Tsolaki 2011; Greece
Objective	This study aimed to examine the effectiveness of a holistic cognitive rehabilitation program on patients with MCI
Methods	Design: RCT Recruitment: outpatients of the memory and dementia clinic of the G Papanikolaou general hospital and day centres of the Greek Alzheimer Association between 2000 and 2008 Exclusion Criteria: stroke history or evidence of ischemic lesions; use of cholinesterase inhibitors; diagnosis of dementia; lack of insight into their deficits and visual/hearing impairment or reading/writing disability sufficient to interfere with training
Participants	Sample: *n* = 196 Intervention *n* = 122; Control *n* = 79 Mean Age (SD): Intervention: 68.45(6.99) years; Control: 66.86 (8.79) years Gender [Female n(%)]: Intervention: 72 (59%); Control: 54 (68%) Loss to Follow-up: Intervention: *n* = 18; Control: *n* = 5
Intervention	Description of Intervention: Therapeutic Techniques of nPhTh: holistic approach including cognitive training, cognitive stimulation and psychotherapeutic techniques Description of Control: no therapy Duration of Intervention: 6 months Length of Follow-up: immediate post
Study/Location	Wei 2014; China
Objective	To examine the effect of handball training on cognitive ability in elderly with MCI
Methods	Design: RCT Recruitment: not reported Inclusion Criteria: aged 60 to 75 years old; existing subjective or objective cognitive impairment; MMSE Score ≤ 26 points, the level of Global Deterioration Scale assessment is between 2 and 3; activity of daily living scale (ADL) Score ≤ 18 points; Hachinski ischemia index (HIS) ≤ 4 points; course of cognitive impairment > 3 months; normal or corrected-to-normal hearing and vision Exclusion criteria: depression (self-rating depression scale standard < 53); history of drug use, such as memory-improving drugs; body movement disorder
Participants	Sample: *n* = 60 Intervention: *n* = 30; Control: *n* = 30 Mean Age (SD): Intervention: 66.73 (5.48); Control: 65.27 (4.63) Gender [Female n(%)]: Intervention: 9 (30%); Control: 11 (37%) Loss to Follow-up: not reported
Intervention	Description of Intervention: 2 groups (15 participants per group) exercised respectively under the supervision of the well-trained nurses for 30 minute/day, 5days/week, for a total of 120 times over 6 months Description of Control: The control group maintained the original life entertainment, such as cards playing,

	etc. Duration of Intervention: 6 months Length of Follow-up immediate post
Study/Location	Winblad 2008; Canada; US
Objective	To determine the safety of galantamine in patients with MCI, its impact on cognition and global functioning, and its potential to delay progression to dementia
Methods	Design: RCT; (2 studies are included in this trial) Recruitment: 7 centres in the US and Canada enrolled participants in both studies Inclusion Criteria: ≥ 50 years with gradual onset and slow progression of declining cognitive ability by history; CDR score of 0.5 and CDR memory score 0.5, and insufficient impairment of cognition and activities of daily living to meet diagnostic criteria for dementia; Delayed Recall score 10 on the New York University Paragraph Recall test; sufficient visual, hearing, and communication capabilities (glasses and hearing aids permitted); willingness to complete serial standard tests of cognitive function; ability to read, write, and fully understand the language of the cognitive scales used; consistent informant accompaniment to scheduled study visits Exclusion Criteria: neurodegenerative disorders or other conditions possibly resulting in cognitive impairment (e.g.,Parkinson disease, Pick's disease, Huntington chorea, cerebral trauma, stroke, hypoxic cerebral damage, vitamin deficiency states, CNS infections, AIDS, brain cancer, significant endocrine or renal disease, or mental retardation); current, clinically significant cardiovascular disease; a history of drug or alcohol abuse; participants with contraindications to the use of MRI
Participants	**Study 1:** Sample: *n* = 990 Intervention: *n* = 494; Control: *n* = 496 Mean Age (SD): Intervention: 69.2 (9.07) years; Control: 70.1 (9.14) years Gender [Female n(%)]: Intervention: 258 (52%); Control: 273 (55%) Loss to Follow-up: Intervention: *n* = 211; Control: *n* = 154 **Study 2:** Sample: *n* = 1058 Intervention: *n* = 532; Control *n* = 526 Mean Age (SD): Intervention: 70.6 (8.65) years; Control: 70.9 (8.72) years Gender [Female n(%)]: Intervention: 293 (55%); Control: 310 (59%) Loss to Follow-up: Intervention: *n* = 215; Control: *n* = 141
Intervention	Description of Intervention: galantamine was administered at 4 mg BID for 1 month, then 8 mg BID for 1 month. If well tolerated, the dose could be titrated to 12 mg BID, but could be lowered back to 8 mg BID after 1 month, if necessary; dose selected at month 3 (8 or 12 mg BID) was fixed for the remainder of the 24-month study Description of Control: placebo Duration of Intervention: 24 months Length of Follow-up immediate post

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