Nutritional interventions for the prevention of cognitive impairment and dementia in East Asia

A systematic review (and meta-analysis)

Aim and objectives

- The aim of this systematic review is to evaluate the current evidence on nutritional interventions in young and older adults for the prevention of dementia and cognitive decline in East Asian Countries.

- Primary outcome:
  - Description of current nutritional interventions for the prevention of cognitive decline and dementia.

- Secondary outcome:
  - 1) study design, sample characteristics, sampling strategies and duration;
  - 2) description of intervention in control group;
  - 3) modalities of delivery of the interventions;
  - 4) attrition rates, compliance and safety of interventions;
  - 5) effect size on outcomes;
  - 6) assessment of strength of evidence and study quality;
  - 7) funding sources and declaration of conflicts of interest.

Protocol systematic review

- **Type of studies:** RCTs

- **Condition studied:** Cognitive impairment and dementia

- **Participants:** Adult participants (age ≥ 18 years) with and without health comorbidities.

- **Interventions:** All interventions with a nutritional component.

- **Context:** Studies conducted in East Asia
  - Malaysia, Thailand, Brunei Darussalam, China, Hong Kong, Indonesia, Myanmar, Papua New Guinea, Philippines, Korea, Singapore, Taiwan, Vietnam, Cambodia, and Laos.

Flowchart

- Literature search in:
  - Embase;
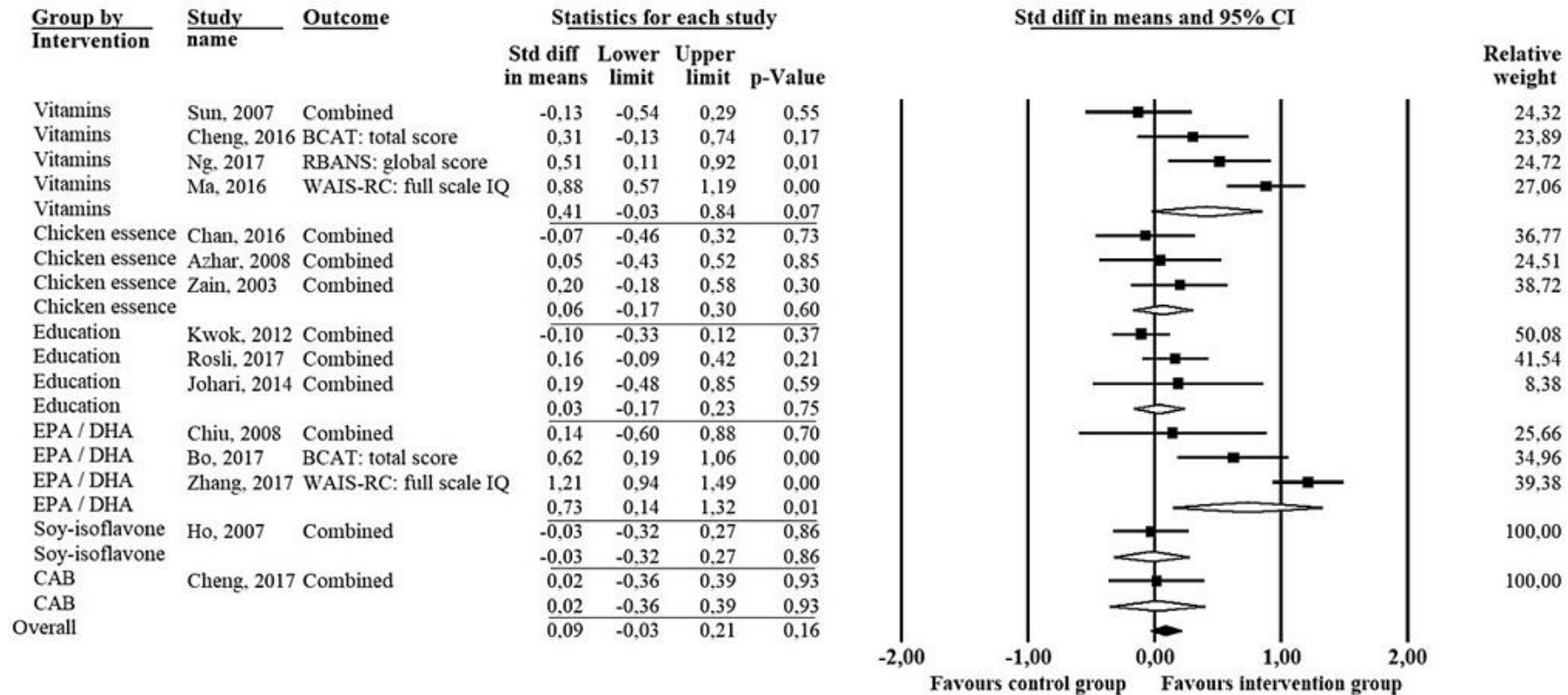 - Medline;
  - Scopus;
  - and PsycInfo.
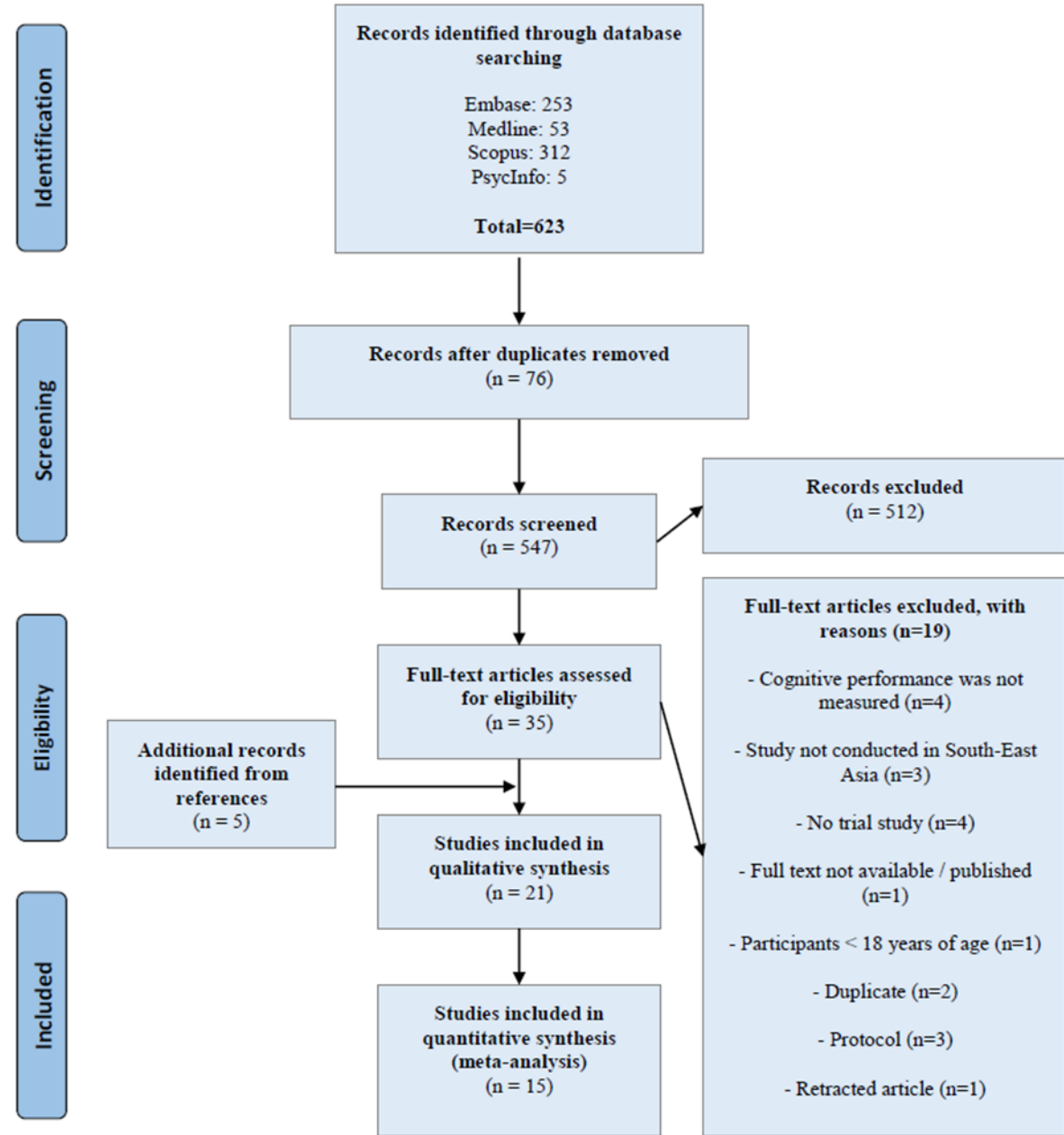
Included studies

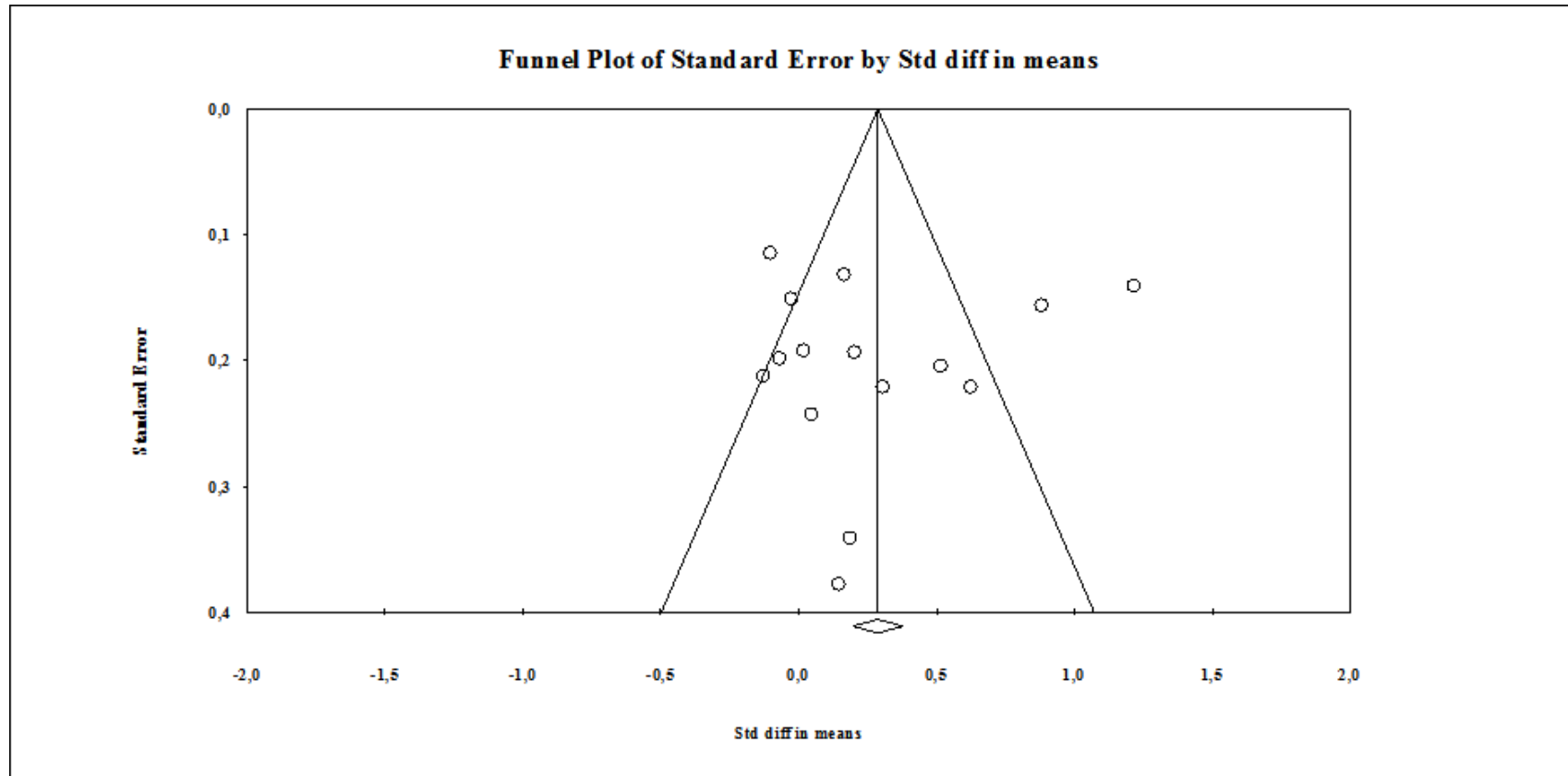**Twenty-one RCTs conducted in South-East Asia.**

- Micro-nutrient supplements [N=6]
- Chicken essence [N=5]
- Nutrition education [N=4]
- EPA / DHA supplements [N=3]
- Soy-isoflavone [N=1]
- L-carnitine [N=1]
- Caffeinated alcoholic beverage [N=1]

Meta-analysis

Effect of nutrition interventions on cognitive performance

Group by Intervention	Study name	Outcome	Std diff in means	Lower limit	Upper limit	p-Value		Relative weight
Vitamins	Sun, 2007	Combined	-0,13	-0,54	0,29	0,55		24,32
Vitamins	Cheng, 2016	BCAT: total score	0,31	-0,13	0,74	0,17		23,89
Vitamins	Ng, 2017	RBANS: global score	0,51	0,11	0,92	0,01		24,72
Vitamins	Ma, 2016	WAIS-RC: full scale IQ	0,88	0,57	1,19	0,00		27,06
Vitamins			0,41	-0,03	0,84	0,07		
Chicken essence	Chan, 2016	Combined	-0,07	-0,46	0,32	0,73		36,77
Chicken essence	Azhar, 2008	Combined	0,05	-0,43	0,52	0,85		24,51
Chicken essence	Zain, 2003	Combined	0,20	-0,18	0,58	0,30		38,72
Chicken essence			0,06	-0,17	0,30	0,60		
Education	Kwok, 2012	Combined	-0,10	-0,33	0,12	0,37		50,08
Education	Rosli, 2017	Combined	0,16	-0,09	0,42	0,21		41,54
Education	Johari, 2014	Combined	0,19	-0,48	0,85	0,59		8,38
Education			0,03	-0,17	0,23	0,75		
EPA / DHA	Chiu, 2008	Combined	0,14	-0,60	0,88	0,70		25,66
EPA / DHA	Bo, 2017	BCAT: total score	0,62	0,19	1,06	0,00		34,96
EPA / DHA	Zhang, 2017	WAIS-RC: full scale IQ	1,21	0,94	1,49	0,00		39,38
EPA / DHA			0,73	0,14	1,32	0,01		
Soy-isoflavone	Ho, 2007	Combined	-0,03	-0,32	0,27	0,86		100,00
Soy-isoflavone			-0,03	-0,32	0,27	0,86		
CAB	Cheng, 2017	Combined	0,02	-0,36	0,39	0,93		100,00
CAB			0,02	-0,36	0,39	0,93		
Overall			0,09	-0,03	0,21	0,16		

Std diff in means and 95% CI

-2,00 -1,00 0,00 1,00 2,00

Favours control group   Favours intervention group

Meta Analysis

Publication bias: meta-analysis

Egger's regression test: 0.43 (1-tailed p-value)

Micro-nutrient supplements: risk of bias

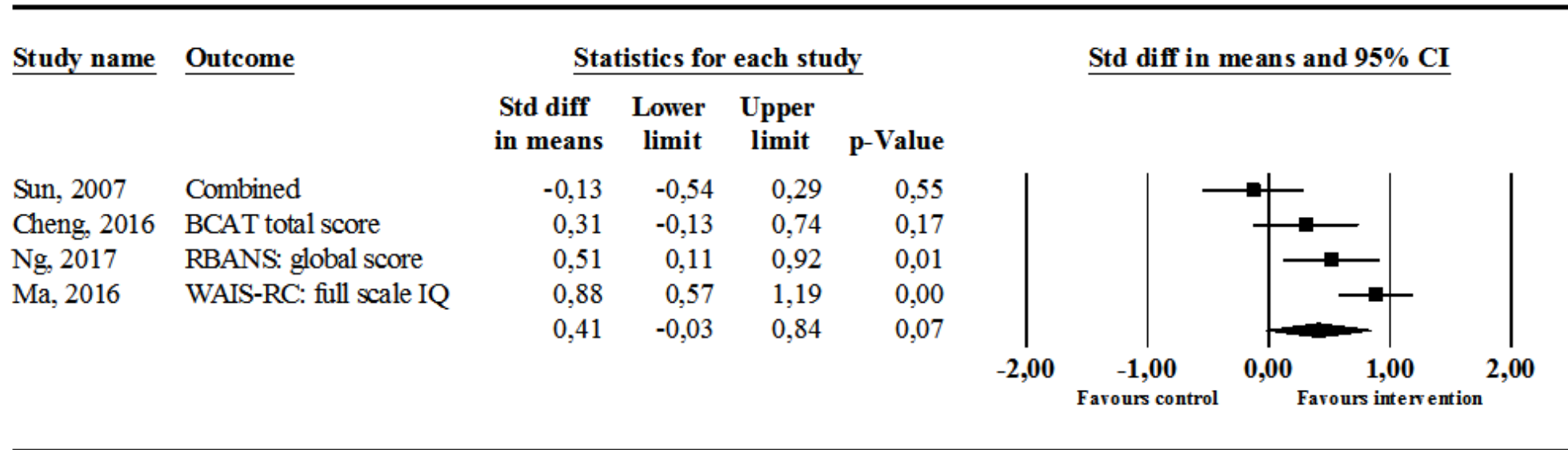|	Sun, 2007	Kwok, 2011	Prado, 2012	Cheng, 2016	Ma, 2016	Ng, 2017
Random sequence generation (selection bias)	+	?	+	?	?	+
Allocation concealment (selection bias)	+	?	+	?	?	+
Blinding of participants and personal (performance bias)	+	+	+	+	+	-
Blinding of outcome assessment (detection bias)	+	+	+	?	?	?
Incomplete outcome data (attriation bias)	+	+	+	-	+	+
Selective reporting (reporting bias)	+	+	+	+	+	+

* Cochrane risk of bias tool

Micro-nutrient supplements: description studies

Author	Sample size	Intervention	Duration	Study group	Country
Cheng, 2016	83	Vitamin B6, B9 and B12	14 weeks	Elderly with elevated homocysteine levels	China
Kwok, 2011	112	Vitamin B9 and B12	104 weeks	Mild to moderate dementia patients	China
Ma, 2016	180	Vitamin B9	26 weeks	Elderly with MCI	China
Ng, 2017	99	Multi-fibre, vitamin B6, B9, B12, D, iron and calcium.	24 weeks	Pre-frail and frail elderly	Singapore
Sun, 2007	89	Vitamin B12 + multi-vitamin	26 weeks	Mild to moderate Alzheimer patients	Taiwan
Prado, 2012	640	Multi-micronutrients	52 weeks	Pregnant women	Indonesia

Micro-nutrient supplements: meta-analysis

Global performance

Study name	Outcome	Std diff in means	Lower limit	Upper limit	p-Value
Sun, 2007	Combined	-0,13	-0,54	0,29	0,55
Cheng, 2016	BCAT total score	0,31	-0,13	0,74	0,17
Ng, 2017	RBANS: global score	0,51	0,11	0,92	0,01
Ma, 2016	WAIS-RC: full scale IQ	0,88	0,57	1,19	0,00
		0,41	-0,03	0,84	0,07

Std diff in means and 95% CI

-2,00   -1,00   0,00   1,00   2,00

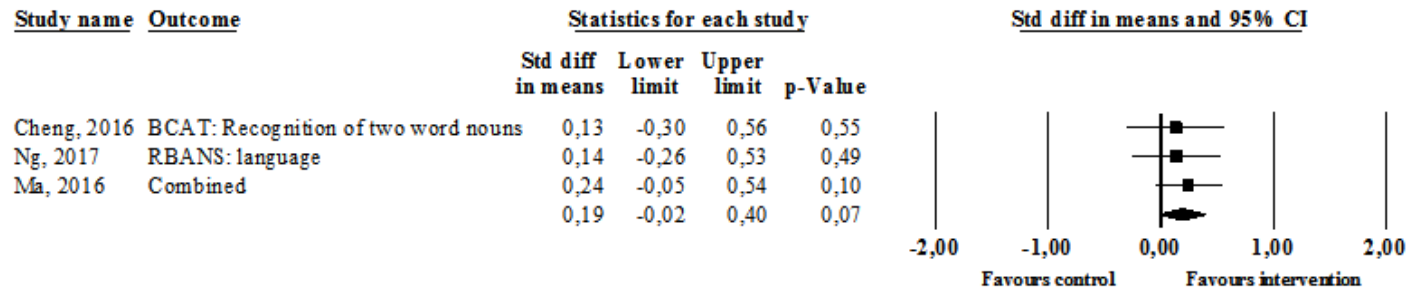Favours control   Favours intervention

Meta Analysis

▪ Random model analysis of global cognitive tests results.

Micro-nutrient supplements: meta-analysis

Verbal functions and language skills

Study name	Outcome	Std diff in means	Lower limit	Upper limit	p-Value	Std diff in means and 95% CI
Cheng, 2016	BCAT: Recognition of two word nouns	0,13	-0,30	0,56	0,55	
Ng, 2017	RBANS: language	0,14	-0,26	0,53	0,49	
Ma, 2016	Combined	0,24	-0,05	0,54	0,10	
		0,19	-0,02	0,40	0,07	

Favours control   Favours intervention

Meta Analysis

Construction and motor performance

Study name	Outcome	Std diff in means	Lower limit	Upper limit	p-Value	Std diff in means and 95% CI
Ng, 2017	RBANS: Visuospatial/constructional	0,23	-0,17	0,62	0,26	
Cheng, 2016	Combined	0,24	-0,20	0,67	0,29	
Ma, 2016	WAIS-RC: block design	0,53	0,23	0,82	0,00	
		0,38	0,17	0,58	0,00	

Favours control   Favours intervention
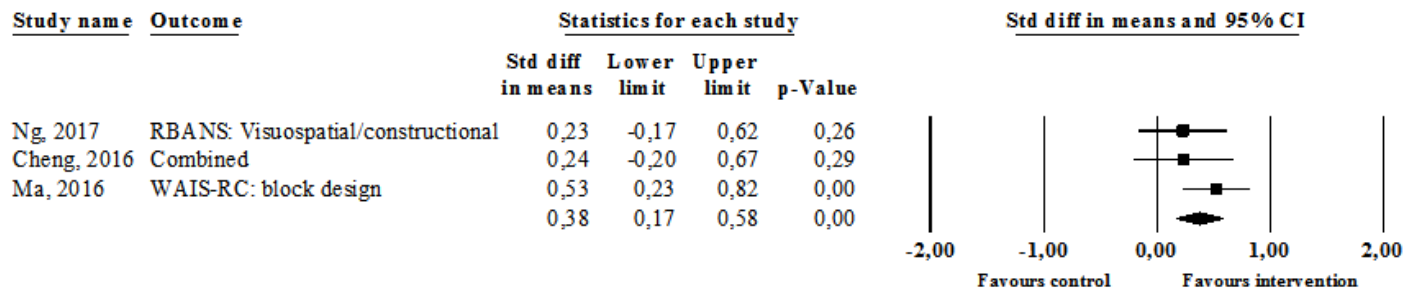
Meta Analysis

- Random model analysis

Micro-nutrient supplements: conclusion

- Limited number of studies.

- However, results indicate that B-vitamin supplementation could prevent cognitive impairment in certain subgroups
  - e.g. elderly with elevated homocysteine levels.

Nutrition education: risk of bias

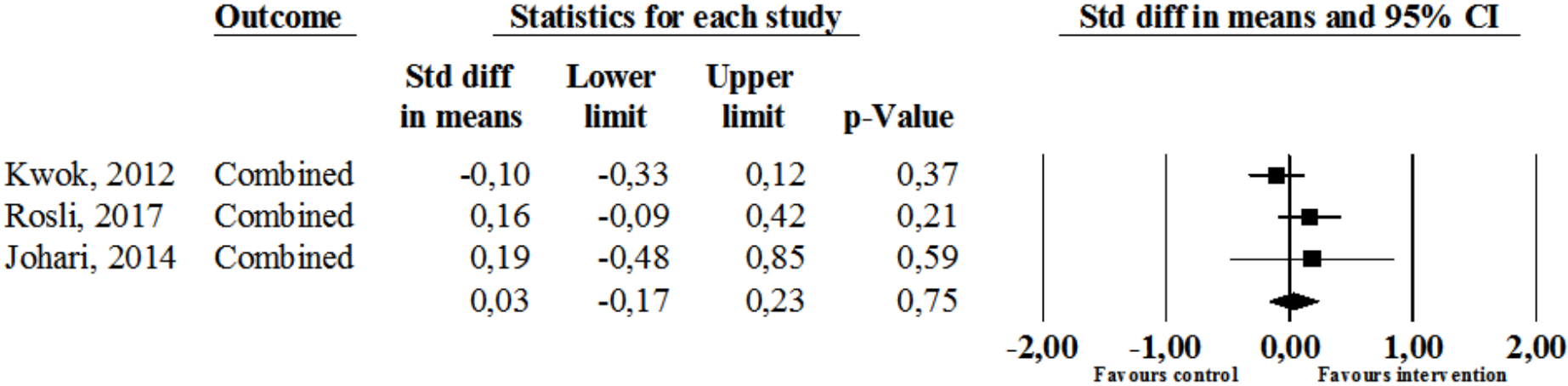|	Kwok, 2012	Johari, 2014	Lee, 2014	Rosli, 2017
Random sequence generation (selection bias)	?	?	+	+
Allocation concealment (selection bias)	?	?	+	+
Blinding of participants and personal (performance bias)	-	-	-	-
Blinding of outcome assessment (detection bias)	+	?	+	+
Incomplete outcome data (attriation bias)	-	+	-	+
Selective reporting (reporting bias)	+	+	?	-

* Cochrane risk of bias tool

Nutrition education: description studies

Author	Sample size	Intervention	Duration	Study group	Country
Johari, 2014	35	Monthly lifestyle and education sessions	12 months	Elderly with MCI	Malaysia
Kwok, 2012	307	Dietary support groups	33 months	Non-demented elderly living in old-age hostels	Hong Kong
Lee, 2014	175	Bimonthly health worker visits, counselling, and rewards to adherence to the program.	18 months	Elderly	Korea
Rosli, 2017	256	Multicomponent group exercises, nutrition education, oral care education, and psychosocial support.	Six weeks	Elderly from poor urban settings	Malaysia

Nutrition education: meta-analysis

Global performance

	Outcome	Statistics for each study				Std diff in means and 95% CI
		Std diff in means	Lower limit	Upper limit	p-Value	
Kwok, 2012	Combined	-0,10	-0,33	0,12	0,37	
Rosli, 2017	Combined	0,16	-0,09	0,42	0,21	
Johari, 2014	Combined	0,19	-0,48	0,85	0,59	
		0,03	-0,17	0,23	0,75	

-2,00   -1,00   0,00   1,00   2,00

Favours control   Favours intervention

Meta Analysis

Nutrition education: conclusion

- Limited number of studies, and large heterogeneity between studies.

- No convincing evidence yet for an intervention, based on promotion of a specific diet, for prevention of cognitive impairment.
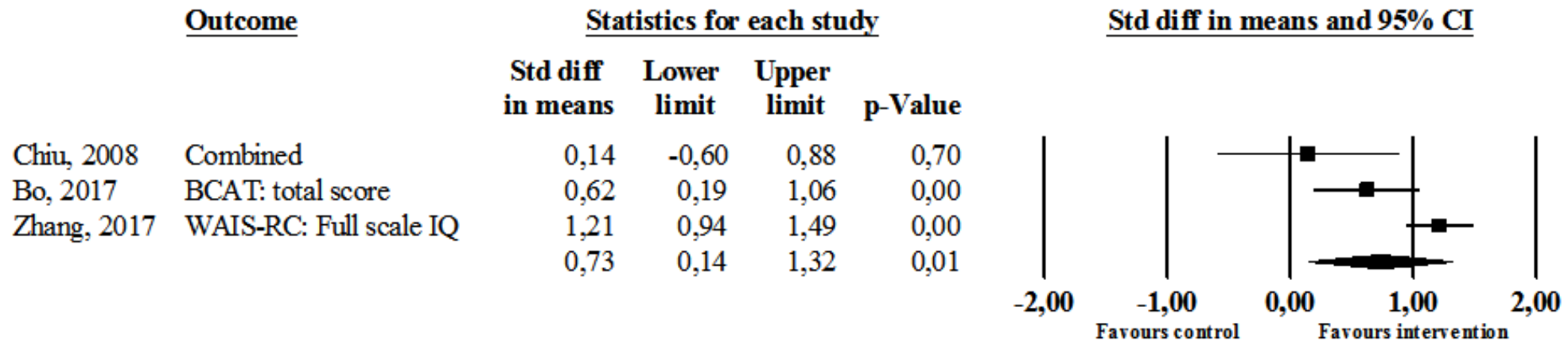
EPA / DHA supplements: risk of bias

	Chiu, 2008	Bo, 2017	Zhang, 2017
Random sequence generation (selection bias)	?	+	+
Allocation concealement (selection bias)	?	+	+
Blinding of participants and personnal (performance bias)	-	-	+
Blinding of outcome assessment (detection bias)	?	?	+
Incomplete outcome data (attriation bias)	+	+	+
Selective reporting (reporting bias)	+	+	+

* Cochrane risk of bias tool

EPA / DHA supplements: description studies

Author	Sample size	Intervention	Duration	Study group	Country
Bo, 2017	86	Daily dosage of 720 mg EPA and 480 mg DHA	Six months	Elderly with MCI	China
Chiu, 2008	29	Daily dosage of 1080 mg EPA and 720 mg DHA	Six months	Elderly with MCI	Taiwan
Zhang, 2017	240	Daily dosage of 2000 mg DHA	Twelve months	Elderly with MCI	China

EPA / DHA supplements: meta-analyis

Global performance

Outcome		Statistics for each study				Std diff in means and 95% CI
		Std diff in means	Lower limit	Upper limit	p-Value	
Chiu, 2008	Combined	0,14	-0,60	0,88	0,70	
Bo, 2017	BCAT: total score	0,62	0,19	1,06	0,00	
Zhang, 2017	WAIS-RC: Full scale IQ	1,21	0,94	1,49	0,00	
		0,73	0,14	1,32	0,01	

-2,00   -1,00   0,00   1,00   2,00

Favours control   Favours intervention

Meta Analysis

EPA / DHA supplements: conclusion

- Limited number of studies.

- Individual studies, and meta-analysis, show positive significant effect of EPA / DHA supplements in elderly with MCI.

- Possibly promising strategy for prevention of dementia in East Asia.

Overall conclusion

- To date, most promising results found for EPA / DHA supplementation, followed by micronutrient supplementation.
    - Large scale studies need to identify into what extend national supplementation policies could lower dementia incidence, and which subgroups need to be targeted.

- In addition, more studies needed to identify the potential of health promotion (nutrition education) for prevention of cognitive impairment in East Asian countries.