Phytochemicals and Cognitive Ageing in Adults Aged ≥ 50 Years

A systematic review and meta-analysis of long-term (≥ 12 weeks) interventions

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AAIC 2026
London | 12-15 July 2026
Abstract #9955
Sunday-0947
Public Health: Population Health Prevention Strategies

Background

Dementia is projected to affect over **150 million people globally by 2050**. The 2024 Lancet Commission identified 14 modifiable risk factors accounting for ~45% of cases, converging on oxidative stress and neuroinflammation as shared pathways.

Dietary phytochemicals modulate these pathways and show neuroprotective effects in preclinical models, but translational evidence from RCTs in adults aged 50 and over remains fragmented.

Objective. To systematically synthesise the effects of phytochemical-rich interventions on cognitive function across five cognitive domains in adults aged 50 and over.

Phytochemical classes examined

- **Anthocyanins** *blueberry, grape*
- **Flavanols / catechins** *matcha, EGCG, ponkan*
- **Carotenoids** *lutein, zeaxanthin, fucoxanthin*
- **Other polyphenols** *chlorogenic acids, quercetin, saffron, raisin*
- **Isoflavones** *fermented soy*

PROSPERO registered | PRISMA 2020 | Cochrane RoB 2

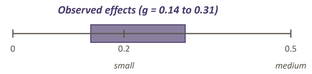
Phytochemicals and the five cognitive domains

Domains ordered by effect size

All five domain-level pooled estimates favoured intervention.

Effects approached but did not reach significance in primary analyses.

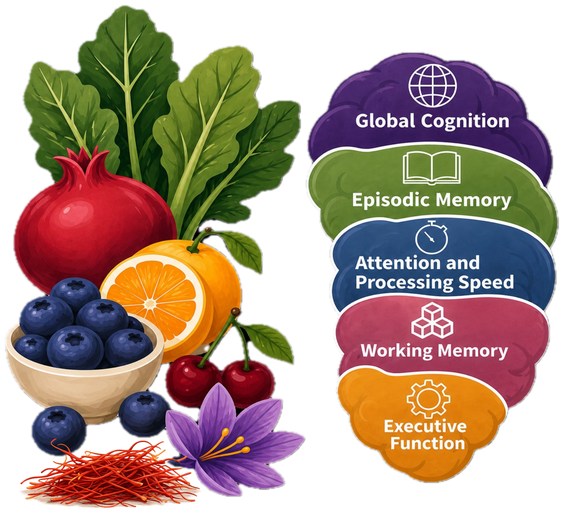
Effect size interpretation *Cohen (1988)*



Proposed mechanisms

- **Antioxidant capacity** *oxidative stress*
- **Anti-inflammatory effects** *neuroinflammation*
- **BDNF / neurotrophic signalling** *synaptic plasticity*
- **Cerebrovascular function** *cerebral perfusion*

> *Effects strengthened in cognitively vulnerable subgroups across independent studies and phytochemical classes.*
>
> *— Convergent finding across 4 independent trials*



Hedges' g [95% CI]

Global Cognition	**0.31** *[−0.00, 0.62]*
Episodic Memory	**0.22** *[−0.01, 0.44]*
Attention and Processing Speed	**0.22** *[−0.09, 0.53]*
Working Memory	**0.17** *[−0.11, 0.45]*
Executive Function	**0.14** *[−0.07, 0.35]*

Methods

Design. Systematic review and random-effects meta-analysis of RCTs.

Search. PubMed, Embase, Scopus, PsycINFO, Cochrane Library (2016–2025).

Inclusion. Adults 50+; oral phytochemical interventions ≥ 12 weeks; validated cognitive outcomes.

Analysis. Hedges' *g* pooled via DerSimonian-Laird random-effects models; I^2 for heterogeneity; sensitivity analyses by risk of bias.

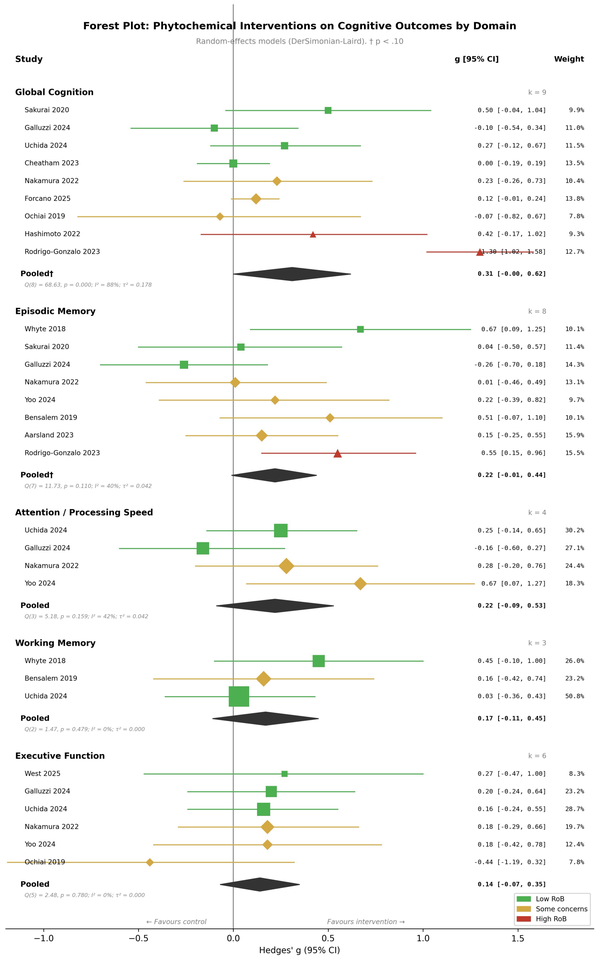
PRISMA flow

16 RCTs | 114 outcomes | ~1,700 participants | 5 domains

Full-text exclusions (n = 7): *age < 50 (2), biomarker-only (1), duration < 12 wk (1), pilot (1), sub-study (1), secondary analysis (1)*

16 RCTs	**114** outcomes
~1,700 participants	**5** domains

Forest plot: pooled effects



Risk of bias: Cochrane RoB 2

Risk of bias domains

Study	D1	D2	D3	D4	D5	Overall
Aarsland 2023	+	+	-	+	-	-
Bensalem 2019	+	+	+	+	-	-
Cheatham 2023	+	+	+	+	+	+
Clark 2025	-	-	-	+	+	-
Forcano 2025	+	+	+	+	-	-
Galluzzi 2024	+	+	+	+	+	+
Hashimoto 2022	X	X	+	-	X	X
Nakamura 2022	+	+	+	+	-	-
Ochiai 2019	-	+	-	+	-	-
Rodrigo-Gonzalo 2023	-	X	+	-	-	X
Sakurai 2020	+	+	+	+	+	+
Sueyasu 2023	+	+	-	+	-	-
Uchida 2024	+	+	+	+	+	+
West 2025	+	+	+	+	-	+
Whyte 2018	+	+	+	+	-	+
Yoo 2024	+	+	+	+	-	-

Domains:
D1: Bias arising from the randomization process.
D2: Bias due to deviations from intended intervention.
D3: Bias due to missing outcome data.
D4: Bias in measurement of the outcome.
D5: Bias in selection of the reported result.

Judgement
X High
\- Some concerns
\+ Low

Most studies (14/16) rated low risk or some concerns. Two studies (Hashimoto 2022; Rodrigo-Gonzalo 2023) rated high risk, driven by deviations from intended intervention and outcome measurement.

Key findings

Domain	k	*g*	I^2	*p*
Global cognition	9	0.31	88%	.052*
Episodic memory	8	0.22	40%	.057*
Attention / processing	4	0.22	42%	.158
Working memory	3	0.17	0%	.233
Executive function	6	0.14	0%	.200

** approaches significance*

Publication bias: Egger's test not applicable (k < 10 per domain)

Sensitivity analysis

When the one high-risk-of-bias trial (Rodrigo-Gonzalo, 2023) was removed, global cognition showed a significant and homogeneous effect:

$$g = 0.11,\ p = .022,\ I^2 = 0\%$$

Convergent pattern of selective benefit

Effects appeared concentrated in cognitively vulnerable subgroups, including APOE-ε4 carriers, baseline decliners, and those with cardiometabolic risk, across independent studies and phytochemical classes.

KEY TAKEAWAY

Phytochemicals deliver small but reliable cognitive gains, which are strongest for global cognition and episodic memory.

Discussion and conclusions

Phytochemical supplementation produces small but consistently positive cognitive effects in adults aged 50 and over, with all five domain-level pooled estimates favouring intervention. Global cognition showed the strongest evidence after excluding high risk-of-bias studies (***g = 0.11, p = .022***). Episodic memory approached significance with the most consistent narrative evidence (5/8 studies positive).

The most clinically meaningful finding may be the convergent pattern of selective benefit in cognitively vulnerable populations. If confirmed in pre-stratified trials, phytochemicals may function as targeted neuroprotective agents rather than broad-spectrum cognitive enhancers, positioning them as candidate components of multi-domain dementia prevention strategies.

Implications for future research. Trials should prioritise enrichment designs targeting at-risk populations, extend follow-up to capture delayed-onset effects, adopt standardised core outcome sets, and characterise bioavailability rather than relying on administered dose. Isolated supplement trials may underestimate the potential of whole plant foods, which contain thousands of bioactive compounds acting synergistically.

Next steps. This synthesis informs a complementary UK Biobank chapter examining habitual whole-food phytochemical intake and cognitive ageing at population scale, advancing convergent evidence across study designs.

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References, funding, contact

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Funding and acknowledgements
Thanks to supervisory team and reviewers for guidance on synthesis methodology.

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