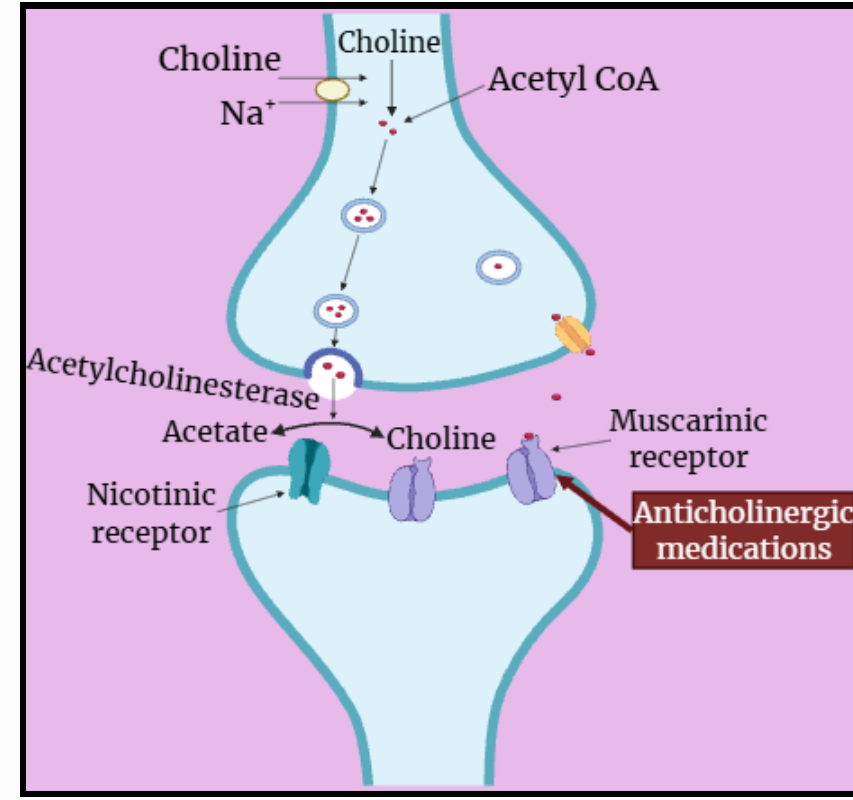


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Background

- Dementia or major neurocognitive disorder (MND): neurodegeneration leading to cognitive decline.¹
- Neuropsychiatric symptoms of dementia (NPS): heterogenous group of behaviors that affect up to 90% individuals with dementia.²
- Psychotropics prescribed for their management lead to anticholinergic effects: dry mouth and impaired cognition.^{3,4}
- Cumulative anticholinergic effect: quantified using anticholinergic burden (ACB).⁴
- While the negative effect of ACB on cognition has been established, effects of ACB on NPS remains unclear.⁵
- Two studies have attempted to evaluate this relationship; however, evidence remains inconclusive.^{6,7}



Objective / Hypothesis

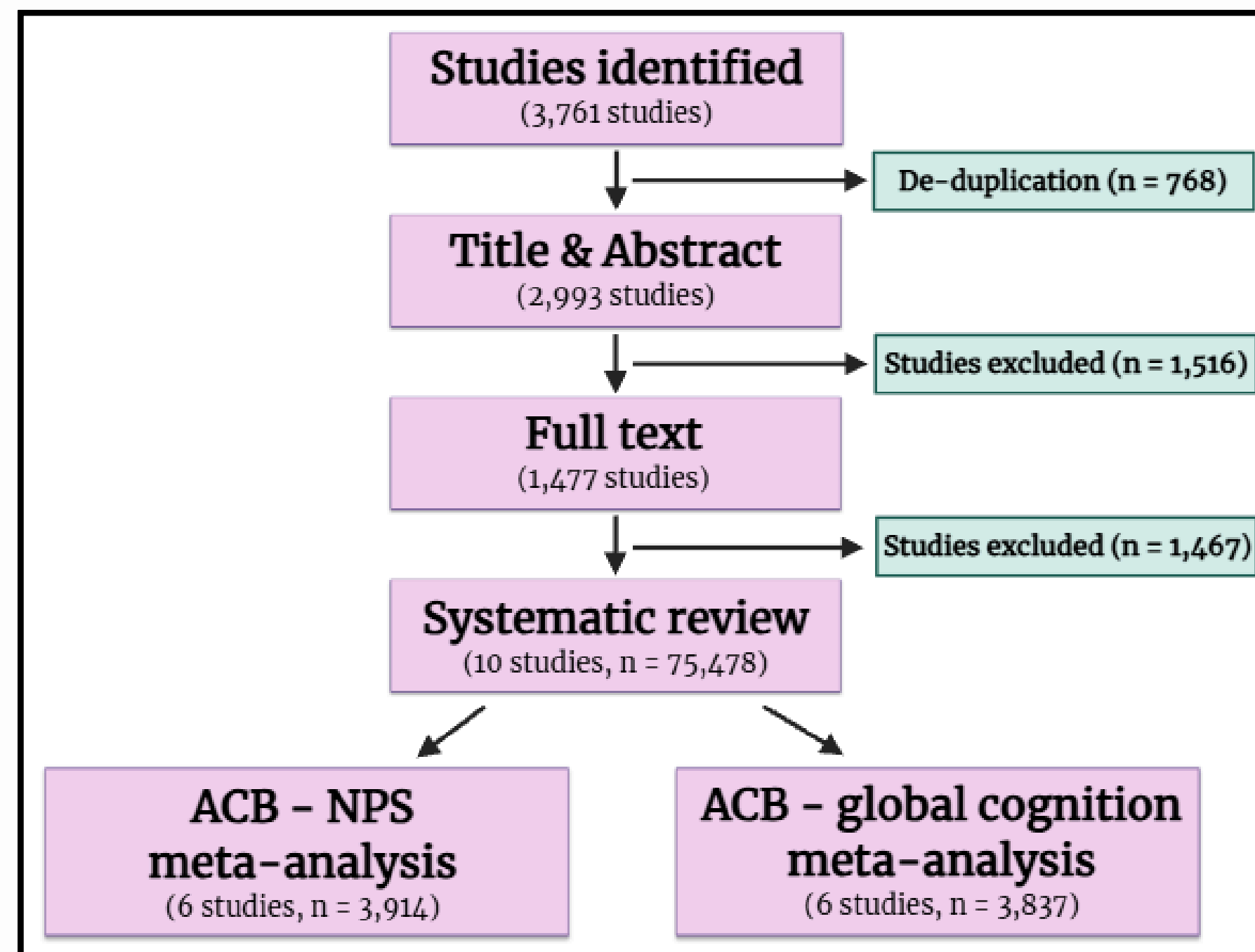
- Objective:** To evaluate the association of ACB with NPS and global cognition in cognitive disorders.
- Hypothesis:** ACB will have a positive association with NPS and a negative association with global cognition.

Methods

- Study registration:** PROSPERO registration number (CRD420251079372).
- Search strategy:** Key domains of “cognitive disorders”, “NPS”, and “ACB”.
- Databases:** PubMed, Web of Science, MEDLINE, Embase, and PsychINFO.
- Filters:** 1st January 2000 to 24th July 2025.
- Search software:** Covidence.
- Title & abstract and full-text screening:** Three reviewers.
- Study inclusion & conflict resolution:** Studies were included upon achieving consensus and discrepancies were resolved by a senior author.

Results

Systematic Search

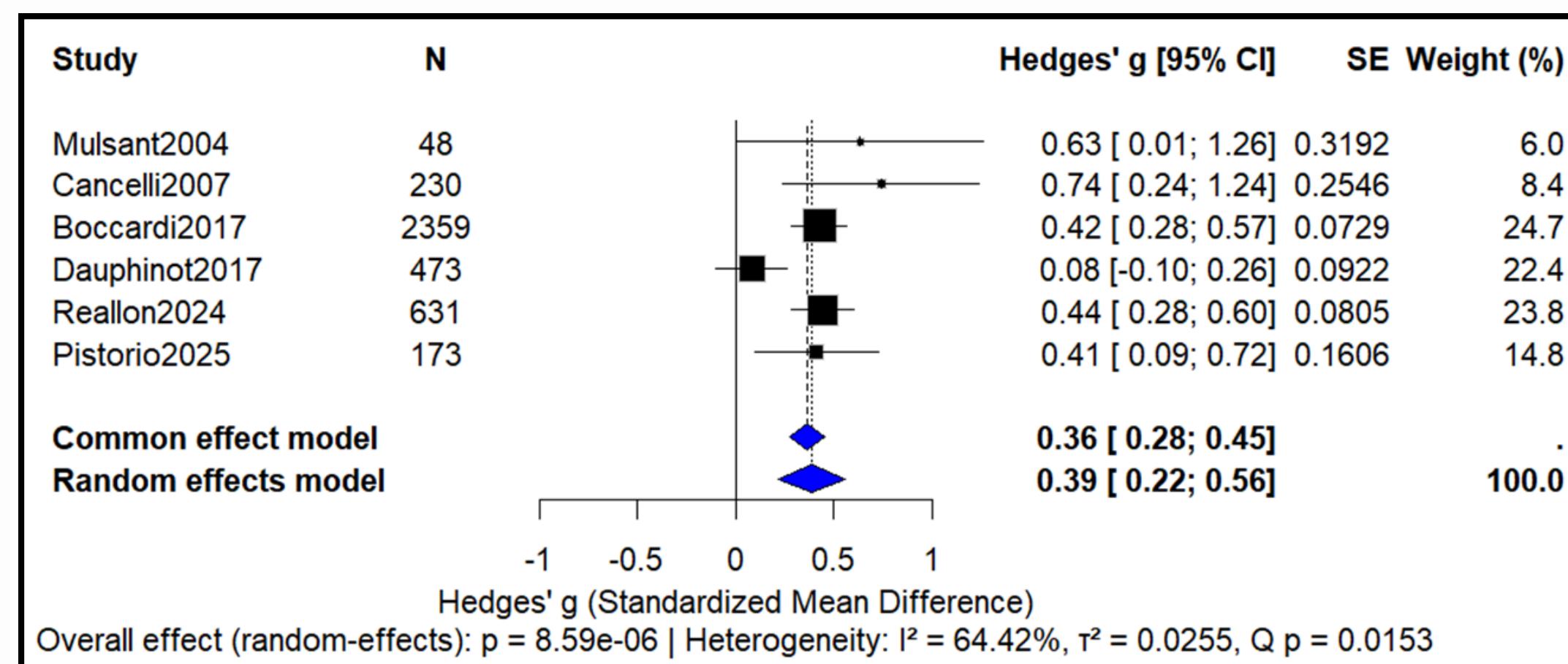


Study Characteristics

- SAA: Serum anticholinergic assay
- ACBS: Anticholinergic cognitive burden scale
- ARS: Anticholinergic risk scale
- DBI: Drug burden index
- NPI: Neuropsychiatric inventory
- BEHAVE-AD: Behavioral pathology in alzheimers disease
- ABS: Aggressive behavior scale

Author (Year)	Sample Size	Country	ACB Measure	NPS Measure
Mulsant <i>et al.</i> (2004)	85	USA	SAA	NPI
Cancelli <i>et al.</i> (2007)	230	Italy	Combination	NPI
Hori <i>et al.</i> (2011)	76	Japan	SAA	BEHAVE-AD
Palmer <i>et al.</i> (2015)	69,877	USA	ACBS	ABS
Boccardi <i>et al.</i> (2017)	2,359	Italy	ARS	NPI
Dauphinot <i>et al.</i> (2017)	473	France	Multiple	NPI
Jaidi <i>et al.</i> (2018)	125	France	ACBS	NPI
Jaidi <i>et al.</i> (2019)	147	France	Multiple	NPI
Reallon <i>et al.</i> (2024)	1,970	France	DBI	NPI
Pistorio <i>et al.</i> (2025)	173	Italy	Combination	NPI

Relationship Between ACB and NPS



- Small - to- moderate effect size (0.39, p < 0.001) and significant heterogeneity (I² = 64.42%, p = 0.015).

Methods (cont.)

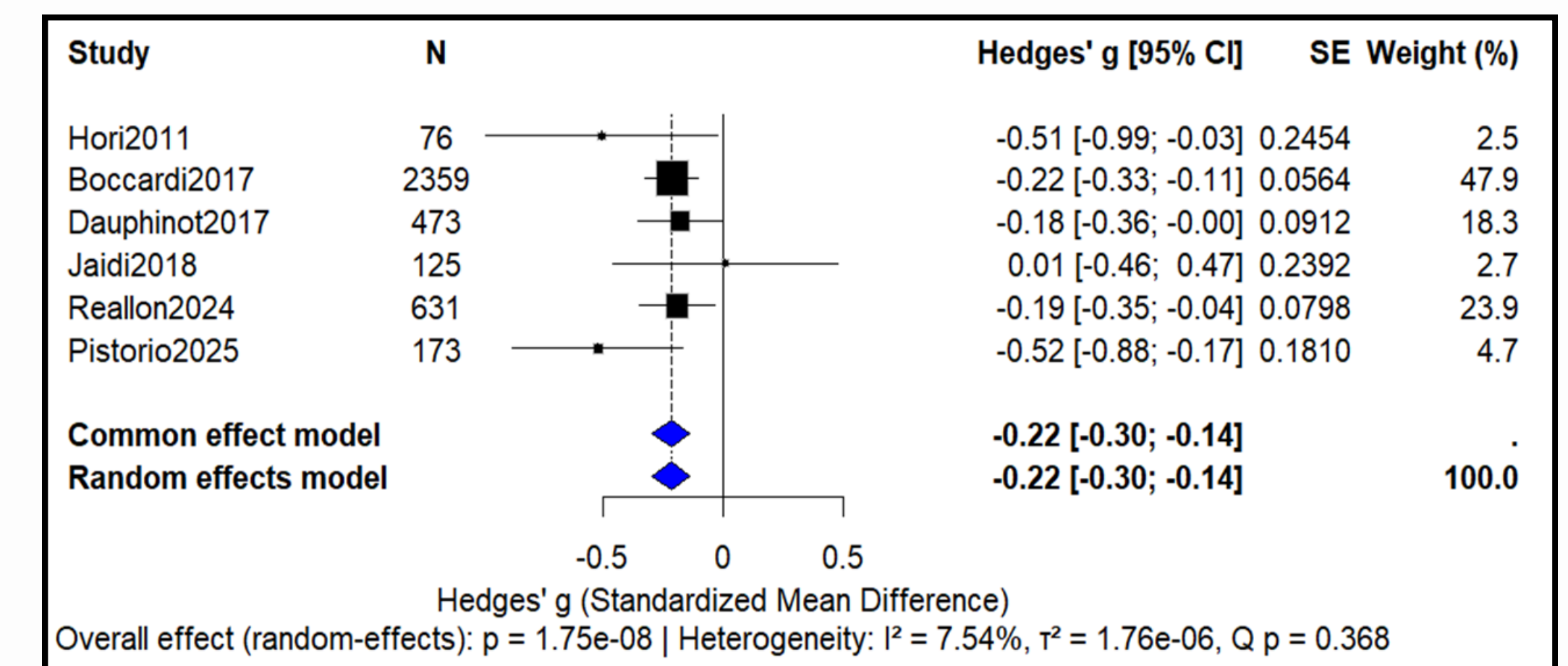
- Eligibility criteria:**
 - Studies published between 1st January 2000 and 24th July 2025.
 - Enrolled participants with neurocognitive disorders.
 - ACB and NPS outcomes were measured using validated instruments.
- Effect size calculation:** Tranformation techniques.^{8,9}
- Risk of bias assessment:** Joanna-Briggs Institute critical appraisal checklist.
- Sensitivity analysis:** Leave-one-out (LOO) analysis (effect size and heterogeneity) and publication bias.
- Certainty of evidence assessment:** Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) approach.

Results (cont.)

Sensitivity Analysis

- LOO (effect size):** Stable effect size range (0.35 - 0.44).
- LOO (heterogeneity):** Moderate overall heterogeneity (I² = 41.80%): 0% (Dauphinot2017) - 54.36% (Mulsant2004).
- Publication bias:** No visual signs; however, formal tests could not be performed (n = 6 studies).

Relationship Between ACB and Global Cognition



- Small-to-moderate effect size (-0.22, p < 0.001). No significant heterogeneity (I² = 7.54%, p = 0.368).

Conclusion / Future Direction

- Higher ACB is associated with more severe NPS and poor global cognition outcomes. Future studies should evaluate this relationship longitudinally.

References

- Jones KC. doi: 10.1176/appi.focus.20210004.
- Cerejeira J, *et al.* doi: 10.3389/fneur.2012.00073.
- Kales HC, *et al.* doi: 10.1136/bmj.h369.
- Bishara D, *et al.* doi: 10.1177/20451253231195264.
- Rahoo R, *et al.* doi: 10.2147/CIA.S541108.
- Wang K, *et al.* doi: 10.1016/j.maturitas.2021.06.004.
- Taylor-Rown M, *et al.* doi: 10.1186/s12877-022-03235-9.
- Wilson DB, George Mason University, 2017.
- Mathur MB, *et al.* doi: 10.1097/EDE.0000000000001105.

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