

Cognitive Efficacy of Cholinesterase Inhibitors and Memantine in Dementia: A Network Meta-Analysis

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Rivastigmine ranked highest for cognitive benefit in mild-to-moderate Alzheimer's disease, galantamine ranked highest in Lewy body/Parkinson's disease dementia, and donepezil was the only agent with consistent benefit in vascular dementia.

INTRODUCTION	METHODS	RESULTS	CONCLUSIONS	REFERENCES
Background: Cognitive outcomes of cholinesterase inhibitors (ChEIs) and memantine have been evaluated across Alzheimer's disease (AD), vascular dementia (VaD), and Lewy body/Parkinson's disease dementias (DLB/PDD). Gap: Head-to-head comparisons across agents, doses, and dementia types are limited, making it difficult to rank treatments for individual patients. Objective: We conducted a network meta-analysis (NMA) to compare and rank cognitive efficacy of ChEIs and memantine across these dementia types and severity strata.	Design: Systematic review and random-effects network meta-analysis of randomized controlled trials (RCTs) identified through May 2025. Included studies: 93 RCTs reporting validated cognitive outcomes in AD, VaD, and DLB/PDD. Outcome measure: Treatment effects were summarized as standardized mean differences (SMDs) with 95% confidence intervals (CIs). Ranking: Treatments were ranked within each dementia category and severity subgroup where data permitted.	AD - overall: Highest-ranked treatments were galantamine 32 mg (SMD 0.69, 95% CI 0.22-1.17), donepezil 27.5 mg patch (SMD 0.54, -0.07-1.15), and rivastigmine 6-12 mg (SMD 0.55, -0.11-1.22). Mild-to-moderate AD: Rivastigmine produced the largest cognitive benefits: patch 10 mg SMD 1.55 (0.87-2.22); tablet 12 mg SMD 1.51 (0.94-2.09). Moderate-to-severe AD: Top-ranked regimens were rivastigmine 12 mg (SMD 0.49, 0.15-0.82), donepezil 5 mg (SMD 0.46, 0.11-0.80), and memantine plus donepezil 10 mg (SMD 0.44, 0.15-0.74). DLB/PDD and VaD: Galantamine 16 mg ranked highest in DLB/PDD (SMD 1.30, 0.47-2.13). In VaD, significant benefits were limited to donepezil 10 mg (SMD 0.34, 0.15-0.53) and donepezil 5 mg (SMD 0.22, 0.06-0.37). Memantine monotherapy: Showed minimal or no benefit in DLB/PDD (SMD -0.38) and VaD (SMD 0.08), and ranked low in mild-to-moderate AD (SMD 0.16).	Differential efficacy: Cognitive efficacy varied substantially across dementia types and severity strata. Top performers: Rivastigmine showed the largest effects in mild-to-moderate AD; galantamine ranked highest in DLB/PDD. VaD: Donepezil was the only treatment demonstrating consistent cognitive benefit in vascular dementia.	Birks JS. Cholinesterase inhibitors for Alzheimer's disease. Cochrane Database Syst Rev. 2006. Tricco AC, et al. Comparative effectiveness of dementia drugs: a network meta-analysis. J Am Geriatr Soc. 2018. Knight R, et al. A systematic review and meta-analysis of the effectiveness of ChEIs and memantine in treating dementia. Dement Geriatr Cogn Disord. 2018. McShane R, et al. Memantine for dementia. Cochrane Database Syst Rev. 2019. CONTACT Moaz Elsayed Abouelmagd Negida Academy, Medical Research Group of Egypt Email: moaz.s.sayed@gamil.com 