

## Efficacy and Safety of Cognitive Enhancers for Mild Cognitive Impairment: A Systematic Review and Meta-analysis

### Highlights and Implications

- A systematic review and meta-analysis of 8 randomized controlled trials and 3 companion reports.
- No improvements in cognition, function or mortality were identified among patients who used cognitive enhancers.
- Numerous harms (nausea, diarrhea, vomiting, headaches) were associated with taking cognitive enhancers.
- Careful consideration needs to be made when determining whether to cover these agents for patients with MCI, given lack of evidence of effectiveness and risk

**Reference:** Tricco AC, Antony J, Soobiah C, et al. Knowledge synthesis methods for integrating qualitative and quantitative data: a scoping review reveals poor operationalization of the methodological steps. *J Clin Epidemiol.* 2016;73:29-35.

**PMID:** [24043661](https://pubmed.ncbi.nlm.nih.gov/24043661/)

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### What is the current situation?

Mild cognitive impairment (MCI) is characterized by memory and cognitive deficits, and increases with age. Between 3% and 17% of MCI cases progress to dementia, a serious public health burden with over 4.6 million new cases a year. Cognitive enhancers, used to treat dementia, are a possible strategy to prevent the progression of MCI, but their efficacy in MCI patients is unclear.

### What is the objective?

This study examines the efficacy and safety of cognitive enhancers for patients with MCI.

### How was the review conducted?

- A systematic review and meta-analysis was conducted; two independent reviewers completed the screening, data abstraction and risk of bias appraisal.
- Selected studies examined MCI patients prescribed donepezil, rivastigmine, galantamine, and/or memantine compared to placebo, other cognitive enhancers and/or supportive care. Outcomes included cognition, function, mortality, and potential harms.

### What did the review find?

- Of the 15, 556 titles and abstracts and 1,386 full-text articles, 8 RCTs (4 examining donepezil 5-10 mg, 2 examining galantamine 16-24 mg, 1 each examining memantine 10-20 mg and rivastigmine 3 -12 mg) and 3 companion reports were included.
- No statistically significant differences were found between cognitive enhancers and placebo across **cognition, function, and mortality** outcomes.
- Patients taking cognitive enhancers experienced significantly more **nausea, diarrhea, vomiting, and headaches** compared to those on placebo. There were no differences in **major adverse events** between those taking cognitive enhancers and placebo.