



Forget about it? Statins and the risk of dementia

CLINICAL QUESTION

Do statins negatively affect cognition, memory, or dementia?

BOTTOM LINE

Randomized controlled trials (RCTs) and large, long-term observational studies suggest no association between statins and risk of dementia or worsening cognition scores.

EVIDENCE

- Previous *Tools for Practice* (published in 2014) found no evidence that statins increase dementia risk or negatively affect cognition.¹ Evidence presented below published since 2014.
- Incidence of Dementia:
 - One systematic review² of RCTs, simvastatin versus placebo.² At 5 years:
 - Incidence of dementia (one RCT, 20,536 patients): 0.3% each group (no difference).
 - Three RCTs³⁻⁵ not in above systematic reviews (732-2,361 patients), statin versus placebo, followed 5-7 years, risk of dementia:
 - Largest RCT: No difference;⁴
 - Smaller RCTs suggest statins reduce risk.^{3,5} Example (732 patients), cognitive impairment incidence: 11% versus 19% (placebo), number need to treat=12.
 - Six systematic reviews⁶⁻¹¹ of observational studies, statin versus no statin (13-46 observational studies, mean age 44-81 years), followed 1-25 years:

- Examples from most reliable systematic review:⁶
 - All-cause dementia (16 studies): Relative risk reduction (RRR) 15%.
 - Alzheimer's disease (14 studies): RRR 28%.
 - Vascular dementia (4 studies): No difference.
 - Other systematic reviews found similar.⁷⁻¹¹
- Cognition Scores:
 - Four systematic reviews of RCT, statin versus placebo in patients with/without baseline cognitive impairment:
 - No difference in Mini-Mental State Examination score,^{2,12-14} Telephone Interview Cognitive Status,² Stroop Word,² Activities of Daily Living score,^{12,14} Alzheimer's Disease Assessment Scale (Cognitive),¹²⁻¹⁴ or Neuropsychiatric Inventory Scale.^{12,14}
 - Two RCTs (described above):⁴⁻⁵ Found similar.
- Adverse Events:
 - Two systematic reviews (2 studies each, 1045-26,340 patients), statins and placebo in patients with/without dementia: No difference.^{2,15}
- Limitations:
 - Most large RCTs evaluating statin cognitive effects are secondary analyses of larger cardiovascular trials.
 - Diagnosis of cognitive decline/dementia varied among trials.
 - Results of observational studies are less reliable due to biases (example, 'healthy user effect': Lower risk patients more likely to use statins).

CONTEXT

- International guidelines vary: Statins have no effect¹⁶ or inconclusive effects¹⁷ on cognition.
- An ongoing community based RCT: Evaluating effects of statins on aging, including dementia. Results expected in 2025.¹⁸

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