Statins and cognitive impairment: Don’t forget the evidence?

Clinical Question: Do statins have any effect on cognitive function or dementia?

Bottom-line: Available evidence indicates that statins do not prevent, treat, or cause cognitive impairment or dementia. The FDA warning seems to be based primarily on case reports that may reflect idiosyncratic short-term “fuzzy” thinking. Decisions to prescribe statins should not be altered.

Evidence:

- Five systematic reviews:1-5
  - Overall [57 studies (19 Randomized Controlled Trials (RCT), 26 cohort, six case-control, six cross-sectional)]:1
    - Incidence of dementia or cognitive impairment:
      - One RCT (20,536 patients): no effect.
      - Observational studies: generally statins reduce the incidence.
        - Example: ten cohort studies (4,360,137 patients), Relative Risk 0.87 [0.82-0.92].
        - These results are less reliable due to biases like lower risk people more likely to use statins.
    - Performance on cognitive function testing:
      - Eighteen RCTs (8,305 patients) including healthy, high cholesterol, or demented patients using a variety of cognitive tests:
        - Of 155 statistical comparisons, 87.7% no effect, 4.5% statin better, 7.7% placebo better.
        - Largest (5,804 patients), mean age 75, non-demented, followed three years: no difference in mini mental state examination (MMSE).
    - Post-marketing surveillance on cognitive adverse events:
      - No difference between statins and clopidogrel or losartan.
      - Statins preventing dementia [two RCTs (26,340 patients)]:2
        - No effect.
        - Limits: cognitive function secondary outcome.
      - Statins treating dementia [three RCTs (748 patients, mean age 79, with probable or possible Alzheimer’s disease, followed ≥6 months)]:3
        - No effect.
        - Trends generally favour statins preventing cognitive decline.
Example: MMSE scores between statin and placebo (mean difference -1.53, (-3.28 to 0.21). Not statistically significant.
Limitations: highly inconsistent results.
  - Two other systematic reviews found similar.4,5

Context:
- In 2012, the U.S. FDA warned that statins may produce cognitive impairment and memory loss/forgetfulness/confusion.6
  - Appears based primarily on case reports.1
  - May be better described as a “fuzzy” or unfocused thinking reaction.6
    - It appears this is idiosyncratic, rare, and resolves when the medicine is stopped.6-8
- It has been proposed that lipophilic statins are more likely to cross blood-brain barrier and may have more central nervous system effects.6,7
  - This is not based on reliable clinical evidence.

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References:

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