The role of lipid-lowering drugs in cognitive function: a meta-analysis of observational studies
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CRD summary
This review looked at the association between lipid-lowering drugs (LLDs) and cognitive impairment (including Alzheimer's disease and dementia). The authors found that types of LLDs called statins seemed to lower the risk of cognitive impairment. These conclusions follow from the limited evidence identified, although some studies finding statins to have no effect might have been missed.

Authors' objectives
To quantify the risk of cognitive impairment with the use of lipid-lowering drugs (LLDs).

Searching
MEDLINE and EMBASE were searched from inception to October 2002; the search terms were reported. The reference lists of retrieved articles were checked and authors of abstracts were contacted for any additional information.

Study selection
Study designs of evaluations included in the review
Studies were included if they reported relative risks (RRs) or odds ratios (ORs), or provided sufficient data to calculate them. No further study design criteria were applied.

Specific interventions included in the review
Studies were included in the review if they described therapy with statins or other LLDs. Details of the specific drugs used in the included trials were not given.

Participants included in the review
The authors did not specify any selection criteria based on participant characteristics. The populations in the included studies were: African-Americans, California residents, UK residents, older adults across Canada, older adults in Pennsylvania, postmenopausal women, and older adults in Illinois and Arizona.

Outcomes assessed in the review
Studies were included if they provided data on Alzheimer's disease, dementia, or cognitive dysfunction. Alzheimer's disease was diagnosed in the selected studies on the basis of the Mini-Mental State Examination, clinical examination, or ICD-9 codes.

How were decisions on the relevance of primary studies made?
Two authors reviewed all studies and any discrepancies were resolved by a third.

Assessment of study quality
The authors did not state that they assessed validity.

Data extraction
Two authors reviewed all studies and any discrepancies were resolved by a third. Data were extracted on: population; the number of cases and/or controls, or cohort size; ORs with 95% confidence intervals (95% CIs) for any LLD; the method of diagnosing Alzheimer's disease; ORs with 95% CIs for statin therapy; and any variables adjusted for.
Methods of synthesis
How were the studies combined?
The authors used a random-effects model to calculate a pooled RR and its corresponding 95% CI.

How were differences between studies investigated?
Heterogeneity was explored using the DerSimonion and Laird Q statistic, graphical techniques, and by calculation of the proportion of total variance of the pooled effect measure due to between-study variance (Ri statistic: see Other Publications of Related Interest).

Results of the review
Seven observational studies were included (more than 62,759 patients): three case-control studies (n=60,222), three cohort studies (n=2,537) and one cross-sectional study.

No significant difference in cognitive impairment was found between users and non-users of LLDs (5 studies; RR 0.62, 95% CI: 0.28, 1.38). Heterogeneity was statistically significant (P=0.03) and was found to be caused by the inclusion of one particular study.

The risk of cognitive impairment in users of statins was significantly lower than in non-users (7 studies; RR 0.43, 95% CI: 0.31, 0.62). No statistically significant heterogeneity was detected (P=0.1).

Authors’ conclusions
LLDs, in particular statins, seem to lower the odds of developing cognitive impairment.

CRD commentary
This review was based on a rather vaguely defined review question that took the interventions and outcomes of interest into account, but did not appear to select studies according to any other major criteria. The sources used to identify relevant literature were appropriate, though it was unclear whether the search was limited to English language studies. The authors do not appear to have searched for unpublished studies and they acknowledged the potential for publication bias. Observational studies, such as those included in this review, are subject to considerable biases and confounding and, although the variables adjusted in each study were listed, no formal validity assessment was carried out.

Some details of the included studies were provided, but more information on the participants and settings might have been helpful. Based solely on the findings of the meta-analysis, the authors’ conclusions that statins may be of benefit and that randomised trials are needed to investigate this in more detail, would appear appropriate. However, the potential for publication bias may mean that the findings (and subsequent conclusions) of this meta-analysis have overstated any possible benefit.

Implications of the review for practice and research
Practice: The authors did not state any implications for practice.

Research: The authors stated that randomised, controlled trials are needed to answer important questions, such as the specific LLD, dosage and duration of therapy for protection against cognitive impairment.

Bibliographic details

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12820814
Other publications of related interest

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Record Status
This is a critical abstract of a systematic review that meets the criteria for inclusion on DARE. Each critical abstract contains a brief summary of the review methods, results and conclusions followed by a detailed critical assessment on the reliability of the review and the conclusions drawn.