B-vitamins and fatty acids in the prevention and treatment of Alzheimer's disease and dementia: a systematic review


CRD summary
The authors concluded that there was insufficient evidence to draw definitive conclusion on the effect of B vitamins and fatty acids for the treatment of cognitive decline, dementia and Alzheimer’s Disease. The authors’ cautious conclusions reflect the limited evidence presented and are likely to be reliable.

Authors’ objectives
To evaluate the effectiveness of B-Vitamins and fatty acids in the prevention and treatment of Alzheimer’s Disease and other forms of dementia.

Searching
PubMed, EMBASE and The Cochrane Library were searched to July 2007; search terms were reported. Bibliographies of relevant publications and systematic reviews were scanned. No language restrictions were applied but studies had to have an English-language abstract.

Study selection
Eligible studies were randomised controlled trials (RCTs) that evaluated the effect of nutrient supplementation on cognitive function in healthy older people or those with cognitive impairment or decline or any type of dementia (including vascular dementia and Alzheimer’s Disease). Nutrients could include single nutrients such as folate/folic acid, other B-group vitamins or fatty acids, simple nutrient combinations, levels of homocysteine and fish consumption. Also eligible were cohort studies that assessed the association of nutrient levels with the risk of developing dementia. The outcomes of interest were change in cognitive performance in RCTs and incidence of dementia or Alzheimer’s Disease in cohort studies. Cross-sectional and case-control studies were excluded.

Most of the RCTs assessed folic acid with or without other B-group vitamins; the others assessed mixed fatty acids. More than half of the cohort studies assessed folate, other B-group vitamins or homocysteine; the rest assessed fish, DHA (docosahexaenoic acid) or EPA (eicosapentaenoic acid). Participants’ ages ranged from 20 to 92 years; most studies included participants over 50 years old. Study duration ranged from four weeks to three years; most studies were of short duration. The level of cognitive decline and measurements used varied between studies (details reported in the review).

One reviewer assessed studies for inclusion and these were checked by a second independent reviewer. Disagreements were referred to the author panel.

Assessment of study quality
Risk of bias in RCTs was assessed using Cochrane Collaboration guidelines and included criteria on randomisation (method of generation and concealment of allocation), similarities at baseline, blinding and losses to follow-up.

The authors did not state how many reviewers assessed study quality.

Data extraction
Data for relevant outcomes were extracted by one reviewer and checked by a second reviewer.

Methods of synthesis
Studies were combined in a narrative synthesis grouped by nutrient supplementation and study design.

Results of the review
Thirty-three studies were included in the review: 14 RCTs (2,438 participants, range seven to 211 participants) and 19 cohort studies (19,485 participants, range 79 to 5,395 participants). The included studies were of variable quality: 10 of
the RCTs reported adequate methods of randomisation and nine reported adequate similarities at baseline and blinding. Losses to follow-up were not reported.

**Folate and other B-vitamins (10 RCTs):** Compared to placebo, folic acid supplementation resulted in a significant improvement in memory and cognitive function in three RCTs but a decline in one cognitive domain was reported in one RCT and one RCT reported no significant differences between groups for folic acid supplementation. No trials reported increased cognitive performance following supplementation with folic acid combined with other B-vitamins (six RCTs) but a trend for increased performance or slower decline was noted in placebo groups compared to intervention groups (three RCTs).

**Fish and fatty acids (four RCTs):** One small RCT reported improvements in cognitive measures between one group that received an intervention and another that received no intervention or placebo (statistical data not reported). One RCT reported improvements in quality of life for the intervention group compared to placebo (statistical data not reported). Two RCTs reported no differences in cognitive function tests between intervention and placebo groups.

The results of the cohort studies are reported in the paper.

**Authors’ conclusions**
There was insufficient evidence to draw definitive conclusions on the effect of B vitamins and fatty acids on cognitive decline, dementia and Alzheimer's Disease; further long-term trials were needed.

**CRD commentary**
The review question was clear with defined inclusion criteria. Several relevant sources were searched. No specific efforts were made to locate unpublished studies so some data may have been missed. Study quality was assessed and some of the results were reported. Appropriate efforts to reduce reviewer error and bias were used for study selection and data extraction; it was unclear whether similar methods were used for quality assessment.

A narrative synthesis appeared appropriate given the differences between studies in terms of interventions and outcome reporting. The included RCTs were mostly small and were of variable quality and relatively short duration, which limited their power to detect any differences in intervention effectiveness that might exist.

The authors’ cautious conclusions reflect the limited evidence presented and are likely to be reliable.

**Implications of the review for practice and research**

**Practice:** The authors did not state any implications for practice.

**Research:** The authors stated that further high quality trials with long term follow-up and clearly defined well-validated outcomes were needed. Future research should include participants with the earliest stages of cognitive impairment.

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