
Vitamin D, cognition, and dementia: a systematic review and meta-analysis

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CRD summary

The authors concluded that lower vitamin D concentrations were associated with poorer cognitive function and a higher risk of Alzheimer's disease. Their conclusion should be interpreted with caution as it was based on evidence from observational studies with potential confounding factors. Their recommendations for further research were appropriate.

Authors' objectives

To examine the association between vitamin D concentration, and cognitive function and dementia, in adults.

Searching

MEDLINE, EMBASE, AMED, PsycINFO, and Cochrane Central Register of Controlled Trials (CENTRAL) were searched for English-language studies, included up to August 2010. Search terms were reported. Reference lists of included articles and previous systematic reviews were searched.

Study selection

Studies, with a comparative group, that examined the relationship between vitamin D and cognition in adults (over 18 years old) were eligible for inclusion. Studies had to report a vitamin D measurement, and use any validated neuropsychological test, such as global function, psychomotor speed, memory, or intelligence, to measure cognitive function, or use any recognised diagnostic criterion for dementia.

Most of the included studies were conducted in Europe or North America. Most participants were living in the community; most were aged 65 years or older; and most were female. Most studies measured 25-hydroxyvitamin D concentration. The studies used various vitamin D cut-off points, various methods of measuring vitamin D, and various cognitive tests.

Two reviewers selected the studies and any disagreements were resolved by consensus.

Assessment of study quality

Study quality was assessed using the Newcastle-Ottawa scale for case-control and cohort studies, the Jadad scale for randomised controlled trials (RCTs), or the QUADAS for diagnostic accuracy studies. Each quality item was rated as met, unmet, or unclear. An overall quality score was not calculated.

The authors did not state how many reviewers assessed quality.

Data extraction

The data were extracted to compare the mean 25-hydroxyvitamin D concentration between groups of patients with Alzheimer's disease and control groups, and to compare the mean Mini-Mental State Examination (MMSE) score between individuals with a vitamin D concentration of less than 50 nanomoles per litre (nmol/L) and 50nmol/L or more. Authors were contacted for missing data.

Two reviewers extracted the data and any disagreements were resolved through consensus.

Methods of synthesis

Pooled weighted mean differences, Hedges' g and 95% confidence intervals were calculated using a random-effects model. Publication bias was assessed with funnel plots. Heterogeneity was assessed using I^2 ; values over 50% were considered to show evidence of heterogeneity. Subgroup and sensitivity analyses were conducted (details in the review).

Results of the review

Thirty-seven studies were included in the review; 21 were cross-sectional, 10 were case-control, one was before-and-after with a comparison group, two were prospective cohort, and three were RCTs. Sample size ranged from 27 to 17,099 participants. Blinding was unclear or unmet in most studies. In 12 of the 21 cross-sectional studies, it was

unclear whether the participants were representative of the population from which they were recruited. Most studies reported or explained the differences between participants with missing data and those with complete data. Two of the three RCTs did not report how the vitamin D was measured.

Cross-sectional and case-control studies: The meta-analysis showed a lower mean 25-hydroxyvitamin D concentration in patients with Alzheimer's disease, compared with controls (WMD -15.0nmol/L, 95% CI -26.2 to -3.9; $I^2=96%$; six studies). When the analysis was restricted to studies using methods other than the Competitive Protein Binding Assay (CPBA), the overall difference was reduced (WMD -6.2nmol/L, 95% CI -10.6 to -1.8; $I^2=1%$; four studies). Similar results were found when studies comparing any dementia against control groups used methods other than the CPBA to measure vitamin D concentration.

The pooled analysis of mean MMSE score showed a higher average score in participants with a 25-hydroxyvitamin D concentration of 50nmol/L or more (WMD 1.2, 95% CI 0.5 to 1.9; $I^2=65%$; eight studies), than in those with less than 50nmol/L. A similar result was found when comparing patients with a vitamin D concentration of less than 25nmol/L against those with 50nmol/L or more. There was no evidence of publication bias.

Cohort studies: Conflicting results were observed on vitamin D and cognitive decline in the two cohort studies.

RCTs: There was no significant difference for the mental assessment score between placebo and supplement (one RCT).

Authors' conclusions

The results suggested that lower vitamin D concentrations were associated with poorer cognitive function and a higher risk of Alzheimer's disease.

CRD commentary

The review question and inclusion criteria were clear. Relevant sources were searched, but there was a possibility that studies were missed as the review only considered articles in English. Unpublished studies were not sought, but the review found no evidence of publication bias.

Appropriate methods to reduce reviewer error and bias were used for study selection and data extraction, but it was unclear if similar methods were used for quality assessment. Study quality was assessed. Statistical pooling might not have been appropriate given the diverse populations, study designs, cognitive tests, confounders, methods used to measure vitamin D, and settings.

The authors' conclusion should be interpreted with caution as it was based on evidence from observational studies with potential confounding factors. Their recommendations for further research were appropriate.

Implications of the review for practice and research

Practice: The authors did not state any implication for practice.

Research: The authors stated that studies should investigate any cause and effect relationship between vitamin D and cognitive impairment. This should be examined over a sufficient period of time, in a large at-risk population.

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