Role of multivitamins and mineral supplements in preventing infections in elderly people: systematic review and meta-analysis of randomised controlled trials

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CRD summary
This review assessed the effectiveness of multivitamins and mineral supplements in reducing infections in elderly people. The authors concluded that the evidence is weak and varies among studies and that further research is required. The methods of the review were not described in full. However, the evidence presented does support the authors’ conclusion.

Authors’ objectives
To assess the effectiveness of multivitamins and mineral supplements in reducing infections in elderly people.

Searching
AMED, Biological Abstracts, British Nursing Index, CINAHL, the Science Citation Index, the Social Sciences Citation Index, the Cochrane Database of Systematic Reviews, EBM Reviews, EMBASE, IBIDS, MEDLINE, NHS Centre for Reviews and Dissemination databases and PREMEDLINE were searched from 1966 to January 2004; the search terms were given. Published reviews, guidelines, Health Evidence Bulletin Wales, conference abstracts and reference lists were also searched.

Study selection
Study designs of evaluations included in the review
Randomised controlled trials (RCTs) were eligible for inclusion.

Specific interventions included in the review
Studies that compared combinations of multivitamins plus mineral supplements with placebo were eligible for inclusion. Studies using single vitamins or minerals were excluded. The included studies used different combinations of supplements (details were reported).

Participants included in the review
Studies in elderly people were eligible for inclusion. In the included studies, the mean age (reported in 6 studies) was over 60 or 65 years; the participants were aged from 50 to 78 years in the other 2 studies.

Outcomes assessed in the review
Studies that assessed infection-related outcomes were eligible for inclusion. In the review, specific measures of infection were determined after reviewing all selected studies. The review assessed the number of days with infection, the proportion of people with at least one infection, the infection rate and adverse events. The included studies assessed different infections (details were reported). The duration of follow-up ranged from 4 months to 2 years.

How were decisions on the relevance of primary studies made?
The authors did not state how the papers were selected for the review, or how many reviewers performed the selection.

Assessment of study quality
Validity was assessed and scored using the Jadad scale, which considers the reporting and handling of randomisation, blinding and handling of withdrawals. The maximum possible score was 5 points. The authors did not state who performed the validity assessment.
Data extraction
The two reviewers extracted the data and resolved any disagreements through discussion. The extracted data included the mean difference between treatments in the number of days with infection, the odds ratio (OR) of at least one infection, and the incidence rate ratio for the difference in infection rates. Where necessary, the authors of primary studies were contacted for additional data.

Methods of synthesis
How were the studies combined?
Separate meta-analyses were conducted for each infection-related outcome. Data were pooled using a fixed-effect method in the absence of significant heterogeneity and a random-effects model when significant heterogeneity was found. Weighted Poisson regression was used to combine continuous outcomes on the mean difference scale, binary outcomes on the (log) OR scale and the incidence rate. Patients in one RCT who were aged under 65 years were excluded from the meta-analysis, but it was unclear whether the reviewers or the authors of the primary study excluded them. There were too few studies to assess publication bias using a funnel plot.

How were differences between studies investigated?
Differences among the studies were discussed with respect to the composition of supplements, the baseline nutritional status of participants and the populations recruited. A sensitivity analysis was conducted for the meta-analysis of the number of days with infection by reanalysing the data, assuming that values reported as standard deviations in the primary studies were actually standard errors. There were too few studies to explore heterogeneity using meta-regression.

Results of the review
Eight RCTs (n=1,303) were included.

All but one of the studies were of reasonable quality, with Jadad scores of 3 or 4 out of a possible 5; the other RCT scored 2, but was only briefly reported.

Supplements significantly reduced the number of days with infection compared with placebo over 12 months. The mean difference based on 3 RCTs was 17.5 days (95% confidence interval, CI: 11, 24, P<0.001). Heterogeneity was present but studies had the same direction of effect. The results were similar after reanalysing the data, assuming that values reported as standard deviations in the primary studies were actually standard errors.

There was no significant difference between supplements and placebo in the proportion of patients with at least one infection. Based on 3 RCTs, the pooled OR using a fixed-effect model was 1.10 (95% CI: 0.81, 1.50, P=0.53).

Supplements reduced the number of infections but the reduction was not statistically significant. Based on 4 RCTs, the pooled incidence risk ratio was 0.89 (95% CI: 0.78, 1.03, P=0.11).

The reporting of adverse events was poor.

Authors’ conclusions
There was weak and conflicting evidence that supplements reduced infections. Further research is required.

CRD commentary
The review question was clear in terms of the study design, intervention and outcomes. The inclusion criteria were broadly defined in terms of participants. Many relevant sources were searched and attempts were made to minimise publication bias. It was not stated whether any language restrictions were applied, thus the potential for language bias could not be assessed. The methods used to select the studies and assess validity were not described, but the authors stated that the review was conducted in accordance with the QUORUM statement. Methods were used to minimise bias in the extraction of data, and validity was assessed using specified established criteria.
Adequate details of each included study were given. The data were combined in a meta-analysis and statistical heterogeneity was discussed for some outcomes. The graphs presented showed between-study heterogeneity in studies included in the meta-analysis of the incidence ratio for infection. The studies had different direction of effect but attention was not drawn to this in the 'Results' section. The evidence presented supports the authors' conclusion that the studies showed weak and conflicting results and that further research is required.

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

**Practice:** The authors stated that there was insufficient evidence to support a policy of recommending the routine use of multivitamin and mineral supplements in elderly people.

**Research:** The authors stated that research is required to assess the effect of multivitamin and mineral supplements on clinical outcomes (using a common definition of infections). Future studies should define the target population (nutritional status, frailty, type 2 diabetes, and so on), use multiple treatment arms to compare different doses of supplements, and have a minimum duration of follow-up of 12 months. The authors also stated that an economic evaluation should be conducted if supplements are found to be effective.

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**Other publications of related interest**

This additional published commentary may also be of interest. Ford Thomas C. Review: multivitamins and mineral supplements do not reduce infections in elderly people. Evid Based Nurs 2006;9:24.

**Indexing Status**

Subject indexing assigned by NLM

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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.