Efficacy of vitamin and antioxidant supplements in prevention of cardiovascular disease: systematic review and meta-analysis of randomised controlled trials


CRD summary
The authors of this review concluded that there was no evidence to support the use of vitamin and antioxidant supplements for the prevention of cardiovascular disease. This review appears to be reliable.

Authors' objectives
To assess the efficacy of vitamin and antioxidant supplements for the prevention of cardiovascular disease.

Searching
The authors searched PubMed, EMBASE, The Cochrane Library, Scopus, CINAHL and ClinicalTrials.gov in June and November 2012, with no language restrictions. The search terms were reported and bibliographies of relevant articles were reviewed.

Study selection
To be included, randomised controlled trials had to report the efficacy of vitamin or antioxidant supplements, for the prevention of cardiovascular diseases, and have a follow-up of at least six months. The relevant outcomes were major cardiovascular events, including cardiovascular death, fatal or non-fatal myocardial infarction, angina, sudden cardiac death, fatal or non-fatal stroke, and transient ischaemic attack.

In the included trials, where reported, the mean age of the participants ranged from 49 to 82 years. Trials were conducted across the world, and assessed a range of supplements. The full details of the supplements and their dosages were given.

Two authors selected studies for the review, with disagreements resolved by discussion or in consultation with a third author.

Assessment of study quality
The Jadad scale was used to rate trial quality. This scale ranges from 0 to 5 points, covering randomisation, blinding and study withdrawal. It appears that more than one reviewer assessed quality.

Data extraction
Relative risks, with associated confidence intervals, were calculated using intention-to-treat data, for each trial. More than one reviewer extracted these data.

Methods of synthesis
Trial data were combined in a series of meta-analyses, using both fixed-effect and random-effects models. Heterogeneity was assessed using I², with over 50% used as the threshold for reporting the random-effects model.

A subgroup analysis was performed for trials with a quality score of 4 or less, and those with a score of 5. Other subgroup analyses were performed by type of prevention (primary or secondary), quality and dose of supplement, type of outcome, study design, duration of treatment, funding source, provider of the supplements, type of control, number of participants (10,000 or more, or under 10,000), and supplements given singly or in combination with others.

Publication bias was assessed using a funnel plot and Egger's test.

Results of the review
Fifty randomised controlled trials (RCTs) were included in the review, with 294,478 participants (range 61 to 39,876). Thirty trials were of primary prevention for a range of populations, including healthy participants and those with a non-cardiovascular disease. Twenty were of secondary prevention for patients with a range of cardiovascular diseases.
Follow-up ranged from six months to 12 years. The mean quality score for 47 trials that were assessed was 4.3 (range 2 to 5). Forty-five trials had blinding and five were open label. Forty-seven trials reported the source of funding. Five trials were funded by pharmaceutical companies and, in 29 trials, the vitamin or antioxidant supplements were provided by the pharmaceutical industry at no cost.

Vitamin or antioxidant supplements were not associated with a reduced risk of major cardiovascular events (RR 1.00, 95% CI 0.98 to 1.02; I²=42%). There was no evidence of publication bias.

There was no benefit from the supplements by type of prevention, type of vitamin and antioxidant, type of cardiovascular outcome, study design, trial quality, duration of treatment, funding source, provider of supplements, type of control, number of participants, and supplements given singly or in combination.

Supplementation was associated with a small increase in the risk of angina pectoris. In high-quality trials, low-dose vitamin B₆ was associated with a slightly lower risk of major cardiovascular events, and vitamin E was associated with a decreased risk of myocardial infarction; these benefits were observed only in trials with supplements provided by the pharmaceutical industry.

**Authors’ conclusions**
There was no evidence to support the use of vitamin and antioxidant supplements for the prevention of cardiovascular disease.

**CRD commentary**
This review had broad inclusion criteria and searching encompassed a range of sources. Quality was assessed and used to test if the overall effect size was robust, by conducting subgroup analyses. More than one reviewer was involved in the review processes, which should minimise bias and errors. Meta-analysis was appropriate and the authors conducted a range of subgroup analyses to assess any potential effects of supplementation.

This review appears to be reliable.

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

**Practice:** The authors stated that governments and regulating agencies for food and drugs should consider vitamin and antioxidant supplements as medicinal products and evaluate their efficacy and safety before marketing them.

**Research:** The authors stated that further randomised controlled trials were needed to confirm any possible increase in the risk of cardiovascular disease with vitamin or antioxidant supplements. Trials were needed for people who were deficient in vitamins or antioxidants at the start, and tools should be developed and validated to assess the quality and bias in each trial.

**Funding**
No grants received.

**Bibliographic details**

**PubMedID**
23335472

**Original Paper URL**
http://www.bmj.com/content/346/bmj.f10

**Indexing Status**
Subject indexing assigned by NLM
MeSH
Antioxidants /therapeutic use; Cardiovascular Diseases /prevention & control; Dietary Supplements; Humans; Randomized Controlled Trials as Topic; Vitamins /therapeutic use

AccessionNumber
12013004926

Date bibliographic record published
23/01/2013

Date abstract record published
30/01/2013

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.