The influence of dietary and nondietary calcium supplementation on blood pressure: an updated metaanalysis of randomized controlled trials
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Authors' objectives
To update the authors’ previous systematic review investigating the effect of calcium supplementation on blood pressure.

Searching
The Cochrane Collaboration strategy (Dickersin 1994, see Other Publications of Related Interest) was used to search for relevant articles. MEDLINE was searched from January 1993 to May 1997. MESH search terms were 'calcium', 'calcium compounds' and 'blood pressure' or 'hypertension', combined with keyword searches of 'randomised controlled trials' and 'meta-analysis' and a text search for the word 'randomised'. EMBASE was searched for the same period using the terms 'calcium carbonate', 'calcium citrate', 'calcium gluconate', or 'calcium and diet' and 'blood pressure' or 'hypertension'. The bibliographies of included studies were searched to identify further relevant studies. Key researchers in the field were contacted to identify additional unpublished data sources. Authors of articles with insufficient data for abstraction were contacted.

Study selection
Study designs of evaluations included in the review
Randomised controlled trials or meta-analyses in which blood pressure was measured in 80% or more of the patients randomised and in which calcium supplements were taken for more than 2 weeks.

Specific interventions included in the review
Calcium supplementation at a level of greater than 1000mg per day, either as a non-dietary intervention in the form of calcium gluconate, calcium carbonate, calcium citrate, calcium citrate malate, or as a dietary supplementation either as a milk/dairy product supplement or through other dietary manipulation.

Participants included in the review
Non-pregnant normotensive or hypertensive patients.

Outcomes assessed in the review
Systolic and diastolic blood pressure.

How were decisions on the relevance of primary studies made?
Two reviewers independently assessed all articles for retrieval. All articles identified as potentially relevant by either reviewer were retrieved.

Assessment of study quality
A methodological quality score was based on the major sources of potential bias and error in the studies. Studies were assessed on the following: concealment of random allocation; blinding of participants, caregivers, and blood pressure measurements; formal training of blood pressure measurers and specification of measurement techniques. Two reviewers independently assessed the validity of each included study.

Data extraction
Two reviewers independently extracted all data, disagreements were resolved by consensus.
Methods of synthesis
How were the studies combined?
A random-effects model was used to combine data from continuous outcome variables. The approach by Fleiss (see Other Publications of Related Interest) was used to account for differences in treatment effects between studies.

How were differences between studies investigated?
A chi-squared test for heterogeneity was conducted and potential sources of heterogeneity were investigated. Possible sources investigated included: age and sex of subjects, normotensive versus hypertensive participants, baseline calcium, dietary versus non-dietary calcium supplementation, and the methodological quality of the studies.

Results of the review
Forty-two randomised controlled trials, 10 of these studies were not included in the earlier review. 10 of the 42 studies presented data in a way which permitted calculation of summary statistics, and 23 of the remaining 31 studies provided additional data that allowed pooling of results. A total of 4560 participants were included in the review, 2068 randomised to calcium supplementation, 2059 receiving no calcium or placebo, and 433 involving cross-over trials in which they received both calcium and placebo.

The pooled analysis of all studies showed a reduction in systolic blood pressure of -1.44 mm Hg (95% CI: -2.20, -0.68, p<0.001) and a reduction in diastolic blood pressure of -0.84 mm Hg (95% CI: -1.44, -0.24, p<0.001). For both estimates of treatment effect evidence of heterogeneity was found at the 5% level. Investigation into the possible sources of heterogeneity showed only significant differences at the 5% level in trials that reported subgroups of hypertensive versus normotensive patients. The summary treatment effect estimates for dietary (n=9 trials) compared to non-dietary (n=33) sources of calcium supplementation showed no evidence for a difference in systolic (p=0.14) and diastolic (p=0.67) blood pressure. There was no evidence of heterogeneity in the dietary trials, but statistically significant heterogeneity at the 5% level remained in the non-dietary trials.

Authors' conclusions
Calcium supplementation from both dietary and non-dietary sources leads to a small reduction in both systolic and diastolic blood pressure. The effect of supplementary calcium in the diet is at least as great as nondietary supplementation.

CRD commentary
A comprehensive review of the area. The literature search was relatively broad although could have benefited from searching further databases. The inclusion and validity criteria were clearly laid out and applied, and details of primary studies were presented. A quality score was assigned to each study however this was not referred to with reference to the study results. Heterogeneity was investigated using appropriate tests, however, a meta-analysis was conducted despite strong evidence of heterogeneity. When significant statistical heterogeneity is found to exist a meta-analysis should not be undertaken, instead a meta-regression, which may control for the various sources of heterogeneity, or a qualitative analysis should be presented.

Implications of the review for practice and research
The authors state that the modest reduction in systolic and diastolic blood pressure do not justify the use of calcium supplementation as a sole treatment for patients with mild hypertension, but do provide support for achieving minimal levels of calcium intake, particularly in vulnerable populations.

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Bibliographic details

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Other publications of related interest

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