Effects of vitamin D supplements on bone mineral density: a systematic review and meta-analysis

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CRD summary

This review concluded that continuing the widespread use of vitamin D for osteoporosis prevention, in adults without risk factors for vitamin D deficiency, seemed to be inappropriate. The authors' conclusions reflect the evidence presented and are likely to be reliable.

Authors' objectives

To evaluate the effects of vitamin D supplements on bone mineral density.

Searching

EMBASE, The Cochrane Library, and Web of Science were searched, without language restriction, up to July 2012, for relevant articles. Search terms were reported. The reference lists from reviews were screened.

Study selection

Randomised controlled trials (RCTs) assessing the effects of vitamin D2 or D3 on the bone mineral density of adults, with no metabolic bone disease, were eligible for inclusion. Interventions could be vitamin D2 or D3, but not a vitamin D metabolite. Trials with co-interventions had to provide the same co-intervention to all groups. The primary outcome of interest was the percentage change in bone mineral density from baseline. Trials of patients with disorders that were likely to affect bone and calcium metabolism, such as chronic kidney disease, pregnancy, or glucocorticoid use, were excluded.

Most of the included trials were of vitamin D3; the remainder were of vitamin D2 or intramuscular vitamin D. The dosages varied. Most trials were placebo controlled; some compared different doses of vitamin D. Most participants were White and female, and their average age ranged from 22 to 80 years. The mean baseline serum 25-hydroxyvitamin D concentration was less than 50 nanomoles per litre, in half the trials that reported it. Bone mineral density was measured at the lumbar spine, femoral neck, total hip, trochanter, total body, or forearm. The trials were conducted in the USA, Bangladesh, Australia, or various countries in Europe, including the UK.

Two reviewers independently selected trials for inclusion.

Assessment of study quality

Trial quality was assessed using the methods from the Cochrane Handbook (no further details were reported). The authors did not state how many reviewers assessed quality.

Data extraction

One reviewer extracted the percentage change in bone mineral density to calculate the mean difference and 95% confidence interval. These data were checked for accuracy by a second reviewer and disagreements were resolved through discussion.

Methods of synthesis

Weighted mean differences and 95% confidence intervals were pooled using a random-effects meta-analysis. Cochran Q and I^2 were used to assess statistical heterogeneity (I^2>50% was deemed significant).

Subgroup analyses were conducted for starting age, vitamin D status, treatment dose, and trial duration. Meta-regression of a number of variables, on the treatment effect, was conducted. A sensitivity analysis excluding trials at a high risk of bias was undertaken.

Publication bias was measured by visual inspection of funnel plots.

Results of the review

Twenty-three RCTs (reporting 24 cohorts) were included in the review, with 4,082 participants. Sample sizes ranged from 45 to 421. Fourteen studies adequately described randomisation; 19 were double-blind; and 10 reported adequate allocation concealment. Completion rates ranged from 61% to 96%.

There was a small benefit at the femoral neck (WMD 0.8%, 95% CI 0.2 to 1.4; 13 cohorts; I^2=67%). There were no statistically significant effects at any other site.

The results of the meta-regression and sensitivity analyses did not significantly alter the main result. The subgroup analyses suggested greater benefits in trials with vitamin D doses of less than 800 international units per day, for the lumbar spine. No other subgroup results were statistically significant.

There was evidence of publication bias for femoral neck and total hip bone density outcomes.

Authors' conclusions

This review found little evidence of benefit, from vitamin D supplementation, for bone mineral density. Continuing widespread use of vitamin D to prevent osteoporosis, in adults with no risk factors for vitamin D deficiency, seemed to be inappropriate.

CRD commentary

The review question was clear, with defined inclusion criteria. Several relevant sources were searched, without language restrictions. No efforts to locate unpublished studies were reported; some evidence of publication bias was seen in the formal analysis.

Study quality was assessed and some results were reported; the RCTs were of variable quality. Appropriate methods to reduce reviewer error and bias were used for study selection and data extraction, but it was unclear if they were for quality assessment. The methods of analysis seem to have been appropriate. Statistical heterogeneity was assessed and factors that might moderate treatment were explored.

The authors' conclusions reflect the evidence presented and are likely to be reliable.

Implications of the review for practice and research

Practice: The authors stated that the widespread use of vitamin D supplements for skeletal protection in adults without specific risk factors for vitamin D deficiency was not justified. Targeting low-dose supplements to those who are likely to be deficient, could free-up substantial resources.

Research: The authors stated that further studies of vitamin D supplements were needed to establish the associations between baseline 25-hydroxyvitamin D concentration and the response to vitamin D supplements.

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