Vitamin D treatment for the prevention of falls in older adults: systematic review and meta-analysis
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CRD summary
This review concluded that vitamin D therapy was effective for reducing falls in older people, although the effect observed was relatively modest. The review was conducted to a good standard and the authors' conclusions are likely to be reliable.

Authors' objectives
To assess the effect of vitamin D treatment on fall prevention in older adults; secondly, to examine whether higher doses of vitamin D were associated with greater benefit.

Searching
MEDLINE, CINAHL, Web of Science, EMBASE, Cochrane Central Register of Controlled Trials (CENTRAL) and LILACS were searched from inception to February 2009; search terms were reported. Bibliographies of selected papers and previous systematic reviews were reviewed for additional studies. No language restrictions were applied, although at least one author had to be able to translate the study.

Study selection
Randomised controlled trials (RCTs) that compared vitamin D therapy with calcium treatment, placebo or no treatment for the prevention of falls in older adults were eligible for inclusion. Vitamin D could be given alone or in combination with calcium. The mean age of trial participants was required to be 60 or over. An explicit definition of a fall and a description of how falls were ascertained were required for trial inclusion. Fall definition was 'unintentionally coming to rest on the ground, floor or other lower level'. The number of participants with one or more fall according to treatment arm, or the relative risk of falling in each treatment arm, also had to be reported. Trials using intramuscular vitamin D were excluded, as were trials restricted to participants with significant neurological disabilities. The primary outcome was the number of participants with one or more falls during follow-up. For trials included in the primary analysis, vitamin D therapy was administered in doses of 200 to 1,000 IU, either as cholecalciferol, ergocalciferol, or alfacalcidol, for a duration of one to 36 months. Trial comparators were either placebo or calcium. Several trials administered adjunctive calcium in the intervention arm; most of these also administered calcium in the control arm. The mean age of trial participants ranged from 71 to 92 years; most were reported to be women. Community-dwelling, institutionalised and hospital-dwelling adults were included. A history of previous fall was reported in 14% to 100% of participants; previous fractures were reported in 5% to 69%. Falls were ascertained by direct observation, questionnaire alone, fall diaries, or a combination of methods.

Two authors independently reviewed the titles, abstracts and full-text manuscripts of relevant articles to assess study eligibility. Disagreements were resolved by consensus and referral to the original papers.

Assessment of study quality
Trial quality was assessed using guidelines from the Cochrane Collaboration. Data were collected on sequence generation, allocation concealment, assessor blinding, incomplete outcome data, selective reporting, eligibility criteria, therapies, excluded patients, and reliability of fall ascertainment.

Two authors conducted the validity assessment independently.

Data extraction
Data were extracted using a standardised form. The relative risk (RR) of falling and 95% confidence intervals (CIs) were extracted.
Two authors independently extracted data; abstracted data were verified by a second reviewer.

**Methods of synthesis**

A random-effects model was used to estimate a summary relative risk for the vitamin D arm (with or without calcium supplementation) versus any comparator. Where multiple doses of vitamin D were evaluated in separate intervention arms, a pooled effect estimate from all arms with vitamin D was compared with a pooled effect estimate from all arms without vitamin D. $I^2$ was used to assess heterogeneity; $I^2$ greater than 50% suggested moderate heterogeneity.

A priori subgroup analyses to explore potential heterogeneity were specified. These included type, dose and duration of vitamin D, use of adjunctive calcium in the intervention arm, type of dwelling, history of fall or fracture in most participants, mean baseline vitamin D level ≤30ng/mL. For trials that compared multiple doses of vitamin D, each arm was compared with the control arm to derive a relative risk of falling for the relevant subgroup analyses.

A meta-regression analysis was performed to examine the linear association between vitamin D dose or duration and treatment effect. Sensitivity analyses were performed on trials with similar baseline characteristics between intervention and control groups.

Publication bias was assessed using funnel plots and the Begg’s and Egger’s statistical tests.

**Results of the review**

Ten RCTs (including 2,932 participants) were included in the primary analysis. A further seven trials were found (with no explicit fall definition); six of these (n=11,812 participants) were included in a secondary analysis. Trial quality was generally good, with adequate description of sequence generation and allocation concealment provided in over half of the trials. All but one trial were double-blinded and intention-to-treat analysis was clearly stated.

Vitamin D supplementation resulted in a reduction in falls of 14% in older adults compared with placebo or calcium alone (RR 0.86, 95% CI 0.79 to 0.93; $I^2$=7%).

Significantly fewer falls were observed in the following subgroups: community-dwelling adults (aged over 80), adjunctive calcium supplementation, no history of fractures or falls, duration of treatment over six months, cholecalciferol and vitamin D dose of 800 IU or more.

No linear association between vitamin D dose ($P=0.13$) or duration ($P=0.38$) and treatment effect was observed in the meta-regression.

Sensitivity analysis including only trials with similar baseline characteristics between groups did not have a large effect on the relative risk estimate (RR 0.81, 95% CI 0.69, 0.94).

There was no evidence of significant publication bias according to the Begg and the Egger tests.

A post hoc analysis including the seven studies with no explicit fall definition led to a smaller but statistically significant reduction in falls and increase in trial heterogeneity (RR 0.92, 95% CI 0.87 to 0.99; $I^2$=36%).

**Authors’ conclusions**

Vitamin D was effective for fall reduction in older adults. It was well tolerated and inexpensive; despite apparent modest effects (possibly due to inadequate dosing), it might lead to significant decreases in the costs associated with fall morbidity and mortality.

**CRD commentary**

The aim and inclusion criteria for this review were clear and appropriate. The literature search included both electronic and manual elements but did not describe any attempt to identify grey literature, so publication bias was possible. No language restrictions were used, which suggested that language bias should not be an issue; however, only studies that could be translated by a review author were included and the eligible languages were not described. Two authors
independently carried out the main stages of the review, which reduced the risk of reviewer bias.

A comprehensive quality assessment was performed with reference to the Cochrane Handbook; the results were discussed in detail, but quality features were not investigated in the subgroup analyses. Results of the quality assessment and other trial and patient characteristics were provided in table format. The statistical synthesis of included trials was appropriate, as were the methods used. The subgroup analyses were well reported.

Overall, the review was carried out to a good standard and the authors’ conclusions followed clearly from the data presented.

Implications of the review for practice and research

Practice: The authors stated that vitamin D supplementation should probably be incorporated into the clinical practice of providers caring for older adults, especially those at risk of falling.

Research: The authors stated that future better powered studies should investigate whether particular populations or treatment regimens may receive greater benefit than others; for example, optimal dose of vitamin D, the sustainability of beneficial effects and its effect in patients who are not deficient in vitamin D, and the effect of vitamin D for reducing falls in hospitalised patients.

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