

Abstract

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Prevention of nonvertebral fractures with oral vitamin D and dose dependency: a meta-analysis of randomized controlled trials.

Bischoff-Ferrari HA, Willett WC, Wong JB, Stuck AE, Staehelin HB, Orav EJ, Thoma A, Kiel DP, Henschkowski J.

Centre on Aging and Mobility, University of Zurich, University Hospital, Switzerland.

BACKGROUND: Antifracture efficacy with supplemental vitamin D has been questioned by recent trials.

METHODS: We performed a meta-analysis on the efficacy of oral supplemental vitamin D in preventing nonvertebral and hip fractures among older individuals (> or =65 years). We included 12 double-blind randomized controlled trials (RCTs) for nonvertebral fractures (n = 42 279) and 8 RCTs for hip fractures (n = 40 886) comparing oral vitamin D, with or without calcium, with calcium or placebo. To incorporate adherence to treatment, we multiplied the dose by the percentage of adherence to estimate the mean received dose (dose x adherence) for each trial.

RESULTS: The pooled relative risk (RR) was 0.86 (95% confidence interval [CI], 0.77-0.96) for prevention of nonvertebral fractures and 0.91 (95% CI, 0.78-1.05) for the prevention of hip fractures, but with significant heterogeneity for both end points. Including all trials, **antifracture efficacy increased significantly with a higher dose and higher achieved blood 25-hydroxyvitamin D levels** for both end points. Consistently, pooling trials with a higher received dose of more than 400 IU/d resolved heterogeneity. For the higher dose, the pooled RR was 0.80 (95% CI, 0.72-0.89; n = 33 265 subjects from 9 trials) for nonvertebral fractures and 0.82 (95% CI, 0.69-0.97; n = 31 872 subjects from 5 trials) for hip fractures. **The higher dose reduced nonvertebral fractures in community-dwelling individuals (-29%) and institutionalized older individuals (-15%), and its effect was independent of additional calcium supplementation.**

CONCLUSION: **Nonvertebral fracture prevention with vitamin D is dose dependent, and a higher dose should reduce fractures by at least 20% for individuals aged 65 years or older.**

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