



Critical Appraisal

Do calcium and vitamin D supplements prevent fractures?

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Porthouse J, Cockayne S, King C, Saxon L, Steele E, Aspray T, et al. Randomised controlled trial of calcium and supplementation with cholecalciferol (vitamin D₃) for prevention of fractures in primary care. *BMJ* 2005;330(7498):1003. Full text available at: <http://bmj.bmjournals.com/cgi/content/full/330/7498/1003>.

Research question

Does giving calcium and vitamin D supplements to community-dwelling older women at increased risk of hip fractures reduce their risk of any fractures?

Type of article and design

Open randomized controlled trial.

Relevance to family physicians

Low-trauma fractures add a great burden of illness and cost to society.¹⁻³ Strategies to prevent the continuing rise in hip and other fractures are needed,⁴ particularly in community settings. Calcium and vitamin D supplements might be a relatively inexpensive way to reduce fracture rates. Previous trials have shown substantial reductions in hip and other fractures among women in nursing homes using these supplements.^{5,6} Vitamin D supplementation has also been shown to reduce falls.⁷ No previous trial, however, has examined reduction in fractures as the main end point among community-dwelling women.

Overview of study and outcomes

Women aged 70 and older with at least 1 self-reported risk factor for hip fracture (body weight <58 kg, previous fracture, maternal history of hip fracture, smoking, and poor or fair self-reported health) were identified at nurse-led primary care clinics. Women were excluded if they could not give written consent; were receiving calcium supplements of more than 500 mg/d; or had a history of kidney or bladder stones, renal failure, or hypercalcemia. The intervention group received general lifestyle advice on how to reduce risk of fractures and a 6-month supply of 1000 mg of calcium (calcium carbonate) and 800 IU of

vitamin D, each as 1 tablet daily. Both control and intervention groups were sent leaflets with general advice on prevention of falls and dietary advice on adequate consumption of calcium and vitamin D.

The main outcome was number of fractures, excluding those of digits, ribs, face, and skull, reported on questionnaires mailed to participants every 6 months and confirmed by physicians. Secondary outcomes included hip fracture alone, quality of life, death, visits to physicians, hospital admissions, and falls and fear of falling.

Results

From September 2001 to November 2002, 3314 women were recruited. Intervention and control groups were balanced for all important predictors of fractures. During a median follow up of 25 months, 149 self-reported fractures were confirmed (4.4% in the intervention group and 4.6% in the control group, adjusted odds ratio [OR] 1.01, 95% confidence interval [CI] 0.71 to 1.43). In analysis of survival, there was no difference between the 2 groups in time to fracture, and no evidence of benefit from supplementation was found in prevention of fractures. Inclusion of all fractures (whether or not confirmed by physicians) did not change the results (adjusted OR 1.60, 95% CI 0.75 to 3.40). Even when the analysis included only women who adhered to the therapy, there was no difference between groups (OR 1.03, 95% CI 0.68 to 1.56).

There was no difference between groups in number of falls, deaths, hospitalizations, and visits to physicians, or quality of life. At 12 months, the rate of adherence among women still alive was 63%.

Analysis of methodology

This open randomized controlled trial studied a self-selected sample of community-dwelling women aged 70 and older with at least 1 risk factor for fracture over a 2-year period. Randomization was computer generated and concealed. Intention-to-treat analysis was used. The strength of an open randomized controlled trial design is that results can be generalized more easily to usual-care settings.

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The study had some methodologic limitations. Control patients were not given placebo and therefore were not blinded to study allocation. Control patients also received general advice on prevention of falls and dietary advice on adequate calcium and vitamin D intake. This might have prompted some control patients to start taking calcium and vitamin D. The authors acknowledged this possible dilution effect but said that it would apply to only 6% of control patients. The study followed women for 2 years, a relatively short time for calcium to affect risk of fractures, given its slow rate of metabolism.⁸ Bone loss has been found to be reduced with calcium and vitamin D supplementation within 1 year, however, in community-dwelling older adults.⁸ Also, the low rate of adherence at 12 and 18 months might have attenuated the effect size.

Outcome data were mainly collected from responses to questionnaires sent to participants every 6 months. Medical records were used only to verify reported fractures, but some fractures might not have been reported, resulting in a lower reported incidence and reduced statistical power. This study focused on calcium and vitamin D supplementation. The authors did not report what other treatment patients were receiving. Given that bisphosphonates are recommended as first-line treatment for osteoporosis, knowing whether patients were taking bisphosphonates would have been helpful for interpreting results.


The 7% volunteer rate of potentially eligible women might have introduced self-selection bias. This bias could have reduced the observed effect size if overall healthier women had volunteered.

Application to clinical practice

In this study, women who were 70 years old or older, weighed less than 58 kg, had previous fractures, had a maternal history of fractures, were smokers, or reported their health to be fair or poor were included, regardless of bone density status or osteoporosis diagnosis. Canadian guidelines recommend screening women older than 65 with any risk factors for osteoporosis and treating women with osteopenia or risk of osteoporosis with calcium and vitamin D (grade B recommendation) as well as bisphosphonates (grade A recommendation). If physicians were following Canadian guidelines, all women in this age group should have been screened for osteoporosis and treated accordingly,⁸⁻¹⁰ but whether the women in this study had been screened and treated is not clear. Canadian dietary guidelines recommend daily intake of 1500 mg of elemental calcium and 800 IU of vitamin D for this age group, based mainly on studies showing that calcium combined with vitamin D reduces bone loss.^{8,9} There is some evidence of the benefit of calcium and vitamin supplementation for fracture reduction as a primary

outcome among women in nursing homes,^{5,6} and secondary analysis of the results of 1 small study has also demonstrated a benefit in the community.¹⁰

Bottom line

- This study found no significant benefit of daily supplementation with calcium and vitamin D for preventing fractures among community-dwelling women 70 years old and older with at least 1 risk factor for osteoporosis.
- The study had reduced statistical power because rates of fracture were lower than expected, possibly due to the heterogeneous sample of women that included some who had had previous fractures and who might have been taking other osteoporosis drugs.
- This study does not support use of 1000 mg/d of calcium and 800 IU of vitamin D supplementation to reduce risk of clinical fractures in postmenopausal women with low bone density. Supplementation with calcium and vitamin D has been shown, however, to increase bone density.
- Physicians should continue to follow the Canadian clinical practice guideline recommendation to prescribe calcium and vitamin D supplementation with bisphosphonates for postmenopausal women with low bone density. 

Points saillants

- Cette étude n'a fait valoir aucun bienfait considérable produit par un supplément quotidien de calcium et de vitamine D pour prévenir les fractures chez les femmes de 70 ans ou plus résidant dans la communauté et ayant au moins un facteur de risque d'ostéoporose.
- La puissance statistique de l'étude était réduite parce que les taux de fracture étaient plus bas que prévu, peut-être en raison de l'échantillon hétérogène de femmes qui incluait certaines ayant eu des fractures antérieurement et qui prenaient peut-être d'autres médicaments contre l'ostéoporose.
- Cette étude ne justifie pas l'administration d'un supplément de 1000 mg/j de calcium et de 800 UI de vitamine D pour réduire le risque de fractures cliniques chez les femmes postménopausiques ayant une faible densité osseuse. Il a cependant été démontré que le supplément de calcium et de vitamine D augmentait la densité osseuse.
- Les médecins devraient continuer à suivre la recommandation du guide de pratique clinique canadien de prescrire un supplément de calcium et de vitamine D avec bisphosphonates pour les femmes postménopausiques ayant une faible densité osseuse.

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