# Should We be Supplementing Calcium? A look at the most recent systematic review with meta-analysis.

"Role of calcium &/or vitamin D Supplementation in preventing osteoporotic fracture in the elderly: A systematic review & meta-analysis." K. Khatri, M. Kaur, T. Dhir, A. Kankaria and H. Arora

Indian J Med Res 2023

Author and Medical Reviewer: Dr. Megan Kimberley, BSc., N.D.

# Supplementation of Calcium and or Vitamin D does not prevent fragility fractures in men and women over 58 years old.

Calcium and Vitamin D, separately or in combination, are usually prescribed to prevent fractures in men and women over 60 years old. This focused review teased out 18 Randomized Controlled Trials (RCT's) from 1987 to 2017 that were selected for low bias, and the specific outcome of preventing a fragility fracture. Combined, this evaluated 39,759 participants responses to doses of calcium carbonate or citrate that ranged from 480mg's to 1,200mg's daily, and vitamin D from 400 IU daily to a single bolus dose of 3,000,000 IU. Sub analysis of dosage differences, interestingly, revealed no significant change in outcomes.

#### Introduction

50 percent of women and 20 percent of men over 50 years old will suffer from an osteoporotic fracture before they die. The appearance of a correlation between increased cardiovascular disease and renal calculi and supplemental calcium is stimulating re-evaluation of this routine clinical recommendation. In the Kuopio Osteoporosis study in 2009, 10,555 women suffered a significant increased risk of coronary heart disease with supplemental calcium and vitamin D (Hazard Ration of 1.24).[1] It must be noted here that the same studies that are recording this nefarious connection are flummoxed at the benign effect of the same amounts of calcium in the diet of those studied.[2] Thus, we return to the question at hand – should we supplement calcium and/or vitamin D to prevent fragility fractures? And if so, when, and how much.

#### Method

The Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) was used to take the initial 1273 studies found down to 18. Search words used over three data bases were "calcium", vitamin D", and "fracture". All studies included had adults older than 50 yrs., with a history of previous fracture. The earliest used RCT was 1987, and the latest few were in 2017. Three ongoing trials were excluded. Cochrane Collaboration's tool was used to filter the quality of studies included. Risk of bias was also thoroughly analyzed, using seven separate bias measures.

The incidence of fracture was measured against calcium and vitamin D, alone or in combination. Each intervention was compared with a placebo or treatment given. Meta-analysis was performed to glean relative risk ratios, absolute risk difference and 95% confidence intervals. Subgroups were specified based on dosages differences, posology, sex, dietary intake, and baseline serum 25(OH)D levels. These subgroups were analyzed, seeking a significance of p < 0.05.

Interventions were vitamin D in daily doses of 400 IU, 1,000 IU, 2,000 IU or 4,000 IU, or single doses of 3,000,000 IU or 5,000,000 IU yearly. Calcium doses used ranged from 480mg's daily to 1,200mg's daily. All interventions were compared to placebo or no treatment.

Countries the studies were conducted in included mostly the United States, United Kingdom, and New Zealand, a couple of Australians, and one Canadian. Included also was a little one from Sweden (50 participants), one big one from Finland (3432 participants), and one from China (312 participants). Participants grand total came to 39,759. Mean age in the studies ranged from 58 to 80 years old.

#### Results

After all this meta-analysis it was concluded that calcium and vitamin D, individually or together, did not lower the likelihood of fragility fractures in

the "elderly" population, being over 58 yrs. Sex, posology, or baseline serum 25(OH)D levels did not significantly affect the outcome.

### Limitations

We are left to assume that the form of vitamin D used was in fact cholecalciferol (D3). Previous studies do show using ergocalciferol (D2), is far less effective at raising serum 25(OH)D.[3]

The form of calcium matters as well. Within these 18 studies, 10 used calcium carbonate. Four of the studies used calcium citrate or citrate malate, and three used lactate and/or gluconate forms. One of the studies used a form that was "unclear" and is therefore unreliably murky. Varying absorbability and tolerability across these forms is debated, but the citrate and malate forms are thought to be more soluble, hence more absorbable, independent of gastric acidity.[4]

### Discussion

The elegance of this systematic review and meta-analysis lies in its focus. The two supplemental interventions were paired as directly as possible with the outcome of importance: patient pain from fractures. Medical Doctors in Canada recommend 1,200mg's of calcium, with vitamin D of varying amounts, to adults over 50 to prevent such pain.[5] Supplemental intake of this calcium and vitamin D enjoys high compliance, as expense is low and marketing successful. The 1,200mg's was taken from The Institute of Medicine Standing Committee on the Scientific Evaluation of Dietary References in 1997.[6] Upon perusal of this document, it is actually 800mg's to 1,200mg's of dietary calcium that is recommended, not supplemental. This amount of calcium hits between the mean and the 75<sup>th</sup> percentile of dietary intake in men and women from 31-50 years old in the United States, and oddly even higher in the "elderly" population (over 58yrs.).

# **Clinical Practice Recommendations**

The following is based on this systematic review and meta-analysis, previous studies, and the authors professional opinion.

1. **Severe Osteoporosis**, in the elderly with concomitant nutritional deficiencies, consider a smaller dose of Calcium Citrate, Malate, or hydroxyapatite 500mg's to 700mg's, with a larger dose of Vitamin D3 1,000 IU to 5,000 IU daily, depending on 25(OH)D serum levels.[2]

- Osteopenic adult patients do better with 50mg's to 200mg's of calcium within a multimineral or multivitamin and mineral daily, with Vitamin D3 at 3,000 IU to 5,000IU (again check serum levels), if any supplement is recommended at all. A balanced diet, and regular weight bearing exercise to individual tolerability works. Reviewing needs for bioidentical hormonal support is also recommended.[7]
- 3. **Prevention**: Healthy balanced nutrition (including fish and green vegetables), and if that is lacking or difficult, recommend a multimineral with calcium (50mgs). Weight bearing physical activity, and sunshine are also proven bone builders, and if that is lacking add vitamin D3 1,000 IU to 5,000 IU, based on serum levels. Reviewing needs for bioidentical hormonal support is also recommended.[7]
- 1. Pentti, K., et al., *Use of calcium supplements and the risk of coronary heart disease in 52-62-year-old women: The Kuopio Osteoporosis Risk Factor and Prevention Study.* Maturitas, 2009. **63**(1): p. 73-8.
- 2. Li, K., et al., *The good, the bad, and the ugly of calcium supplementation: a review of calcium intake on human health.* Clin Interv Aging, 2018. **13**: p. 2443-2452.
- 3. Romagnoli, E., et al., *Short and long-term variations in serum calciotropic hormones after a single very large dose of ergocalciferol (vitamin D2) or cholecalciferol (vitamin D3) in the elderly*. J Clin Endocrinol Metab, 2008. **93**(8): p. 3015-20.
- 4. Bo-Linn, G.W., et al., *An evaluation of the importance of gastric acid secretion in the absorption of dietary calcium.* Journal of Clinical Investigation, 1984. **73**(3): p. 640-647.
- 5. Health Canada, *Dietary Reference Intakes Tables.* . 2006, Food Nutrition: <u>website</u>.
- 6. Institute of Medicine Standing Committee on the Scientific Evaluation of Dietary Reference, I., *The National Academies Collection: Reports funded by National Institutes of Health*, in *Dietary Reference Intakes for Calcium, Phosphorus, Magnesium, Vitamin D, and Fluoride*. 1997, National Academies Press (US) Copyright © 1997, National Academy of Sciences.: Washington (DC).
- Sh7. Shah, N. and D. Ariel, *The role of menopausal hormone therapy in the prevention and treatment of low bone density in perimenopausal and postmenopausal women*. Curr Opin Obstet Gynecol, 2023. **35**(2): p. 141-149.