

## **CALCIUM AND VITAMIN D: *What have we learnt from the Women's Health Initiative Study?***

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There are many therapies that reduce the risk of fracture in postmenopausal women, but all have calcium and vitamin D as co therapies. The role of calcium and vitamin D as a sole therapy for the prevention of fractures is uncertain. Nevertheless, it is estimated that the cost of calcium alone in the USA in 2004 was as high as US\$993 million.

Calcium and vitamin D have been shown to result in small increases in bone mineral density in elderly women, but has minimal benefit in preventing bone loss at the menopause when bone turnover is increased. When calcium and vitamin D3 (800 IU/day) was administered to vitamin D deficient women living in Nursing Homes, it resulted in a 30% reduction in fracture rates. And when administered to individuals with severe vitamin D deficiency, it can significantly increase bone density by more than 40%. Vitamin D is also important for muscle function and supplements have been shown to reduce falls. However, the benefit of calcium and vitamin D in vitamin D replete individuals appears less convincing.

The Women's Health Initiative Study recruited 68,132 women aged 50-79 years living in the USA between 1995 and 2000 to study a number of issues related to women's health. The first of the publications reported on the role of estrogen and progestins for fracture prevention and were published in 2003. This led to major changes in the prescribing of HRT for women. In the calcium and vitamin D arm of this study, the hypothesis tested was to ascertain whether postmenopausal women randomly assigned to calcium and vitamin D would have a lower risk of hip fracture or any other fracture as compared to women receiving placebo.

### The Cohort:

1. In the study, 18,176 women were assigned to active treatment (500 mg calcium carbonate and 200 IU vitamin D3) and 18,106 to placebo.
2. Women were generally younger than in other studies, with a mean age of 62 years. They were also overweight with a mean body mass index of 29 kg/m<sup>2</sup>. Their oral daily calcium intake was high with a mean value of 1150 mg/day (as compared to 400-500 mg in Australian studies). More than half the women (52%) were also taking HRT, with approximately 1% also using other anti-osteoporotic agents.
3. 76% of the women were adhering to therapy and were taking the medicine at the end of the study.

### Bone Density Results:

A subgroup of 2431 women underwent BMD testing. The hip BMD was 1.06% higher in the women taking the active treatment, with non-significant benefits seen in the spine BMD.

Hip and Other Fractures:

During a mean of 7 years of observation:

1. 2102 fractures (including 175 hips) occurred in the women assigned to calcium and vitamin D.
2. 2158 fractures (including 199 hips) occurred in the women assigned to placebo.
3. Annualised fracture rates per 10,000 women years were:

<b>Fracture type</b>	<b>Ca + D</b>	<b>Placebo</b>	<b>(P-value)</b>
Hip	14	16	(0.88, no benefit)
Lower arm/ wrist	44	44	(1.0, no benefit)
Clinical spine	14	15	(0.9, no benefit)
Total	164	170	(0.96, no benefit)

4. A significant reduction in hip fracture (29%), however, was seen in women who were adherent to at least 80% of their active calcium and vitamin D supplements.
5. A significant reduction in hip fracture (21%) was also seen in elderly women aged 60 years or older.
6. No data was available as to the number of women who were vitamin D deficient.
7. No significant risk or benefit was seen with relationship to other major disease outcomes such as heart disease or cancer.
8. There was an increased risk of kidney stones of approximately 17% (449 women in the active and 381 women in the control group) in women receiving calcium and vitamin D.

**CONCLUSION:**

Among healthy postmenopausal women, calcium and vitamin D supplementation resulted in a small but significant increase in hip BMD, but did not significantly reduce hip fracture. An increased risk in kidney stones was noted.

The lack fracture reduction with calcium and vitamin D in this study must be related to the differences in the cohort treated (“healthier, heavier and more dietary calcium”) and the lower dosage of vitamin D used (only 200 IU/day)

(Summarised from Jackson et al, N Engl J Med 2006;354:699-83.)