*Age and Ageing* 2006; **35:** 482–486
doi:10.1093/ageing/afj080
Published electronically 26 April 2006



# Vitamin D supplementation and the prevention of fractures and falls: results of a randomised trial in elderly people in residential accommodation

MALCOLM LAW[1], HEATHER WITHERS[1], JOAN MORRIS[1], FRAZER ANDERSON[2]

[1]Centre for Environmental and Preventive Medicine, Wolfson Institute of Preventive Medicine, Barts and The London, Queen Mary's School of Medicine and Dentistry, Charterhouse Square, London EC1M 6BQ, UK
[2]Geriatric Medicine Group, University of Southampton Medical School, Southampton SO16 6YD, UK

Address correspondence to: M. Law. Email: m.r.law@qmul.ac.uk

## Abstract

**Objectives:** to determine whether vitamin D supplementation reduces the risk of fracture or falls in elderly people in care home accommodation.
**Design:** a randomised controlled trial of cluster design.
**Setting and subjects:** 223 residential units (mainly identical 30-bedded units), within 118 homes for elderly people throughout Britain, with 3,717 participating residents (76% women, average age 85 years). The units provided mainly or entirely residential care (35% of residents), nursing care (42%) or care for elderly mentally infirm (EMI) residents (23%).
**Methods:** participants were randomly allocated by residential unit (cluster design) to a treated group offered ergocalciferol 2.5 mg every 3 months (equivalent to a daily dose of 1,100 IU), or to a control group. Fractures were reported by staff and confirmed in hospital, and routinely collected data on reported falls were obtained.
**Results:** after median follow-up of 10 months (interquartile range 7–14 months), 64 (3.6%) of 1,762 vitamin D-treated residents and 51 (2.6%) of 1,955 controls had one or more non-vertebral fractures, and 24 (1.3%) and 20 (1.0%), respectively, had a hip fracture. The proportion reporting at least one fall was 44% in vitamin D-treated and 43% in control residents. The differences between the vitamin D and control groups were not statistically significant. The incidence of all non-vertebral fractures in the care homes (3.2% per year) and of hip fractures (1.1% per year) was low, similar to rates in elderly people in sheltered accommodation, and the pre-treatment serum 25-hydroxy vitamin D concentration was high [median 47 nmol/l, measured in a 1% ($n = 18$) sample].
**Conclusions:** we found no evidence that vitamin D prevents fractures or falls in elderly people in care home accommodation.

Keywords: *vitamin D, fractures, hip fractures, falls, elderly, prevention*

## Introduction

There is conflicting evidence over whether vitamin D supplementation, with or without calcium, reduces the incidence of fractures in elderly people. Two randomised controlled trials have shown a lower incidence of hip and other long bone fractures in participants receiving calcium and vitamin D supplementation than in controls [1, 2], and three trials have shown a lower incidence with vitamin D alone [3–5]. Conversely, in other trials, fracture incidence was no lower either with calcium and vitamin D [6–8] or with vitamin D alone [8–11] than in controls. The reason for the apparent heterogeneity is uncertain, but one possible explanation is that vitamin D supplementation may be more effective in people living in residential care, perhaps because of a lower dietary vitamin D intake [7]. We present the results of a randomised trial of vitamin D conducted in 3,700 elderly people living in residential accommodation.

Fracture risk is a product of the risk of falling and the structural integrity of bone (usually measured as bone mineral

density). The previous expectation that vitamin D may have a substantial (25% or so) effect in preventing hip fracture was based not only on its effect in preventing loss of bone density (which is modest [12, 13]), but also on a view that vitamin D also prevents falls. This view was supported by observations that muscle weakness, predisposing to gait instability, occurs in people with very low serum levels of vitamin D and improves with vitamin D replacement therapy [14–16]. Falls and fractures are common in elderly people in residential care [17–21], so vitamin D may be effective in this setting.

## Methods

### Study population

The trial was conducted in collaboration with British United Provident Association (BUPA). BUPA Care Homes are the largest provider of residential care homes for elderly people in Britain: 118 homes throughout Britain participated. Residents were eligible to participate in the trial if they were ≥60 years old. Exclusions were temporary residents admitted for respite care, residents who were already taking calcium/vitamin D or drugs that increase bone density (such as bisphosphonates), and residents who had sarcoidosis or malignancy or other life-threatening illness. Data on residents who were ineligible or who declined to participate (including the numbers of such residents) were not available to us. In the case of residents who had confusional states or dementia, the next of kin originally nominated by the resident provided written assent on the resident's behalf. General practitioners (GPs) were informed of their patients' participation in the trial. After receiving training in the study protocol, care home staff invited eligible residents to participate in the trial.

### Ethical approval

Ethical approval was granted by the London Multicentre Research Ethics Committee and by 78 Local Research Ethics Committees. Residents gave written consent to participate.

### Study design

Cluster randomisation by computer was performed. Most of the care homes contained two or more identical and geographically separate 30-bedded units and these provided the randomisation units. Homes without separations tended to be small and for these the entire home was a randomisation unit. There were 223 such units within the 118 homes. Cluster randomisation based on these 223 units was preferred to individual randomisation because it was administratively easier for staff for all residents in a unit to be in the same group (treated or control), and it avoided contamination whereby residents allocated to the control group might inadvertently be given vitamin D. The units were of three types, those in which all or most persons had residential care, nursing care or were elderly mentally infirm (EMI); the proportions of trial participants in the three types of unit were 35, 42 and 23% respectively.

### Intervention

Residents in the units allocated to receive vitamin D were given tablets containing ergocalciferol 2.5 mg [Norton Healthcare (now Ivax Pharmaceuticals)] every 3 months; this is equivalent to a daily dose of 1,100 IU. Previous studies have established that 3-monthly treatment at this dosage is sufficient to maintain elevated serum vitamin D until the next dose [4, 22, 23]. Residents in the control group took no vitamin D (there was no placebo).

### Outcome measures

These were non-vertebral fractures and falls. Fractures were reported by care home staff and confirmed in hospitals. Falls were routinely recorded; a policy of recording all falls in an accident book maintained in each unit was in operation before the trial commenced and these books were the source of our data on falls. The care home staff who recorded the falls were not told that falls were an outcome measure in the trial in order to avoid possible biased recording. Fractures and falls were recorded on all participants originally allocated to the treatment and control groups (intention to treat analysis), up until the time that the trial was terminated or the participant died or left the care home to live elsewhere; care home managers informed us of all participants who died or left the home.

### Blood samples

Blood samples were collected in the care homes from 18 treated group participants (a 1% sample) on three occasions—immediately before the first dose of vitamin D, 1 month after the first dose and 3 months after the first dose (immediately before the second dose). The 18 participants were from five homes in different counties in the south of England; the first dose of vitamin D was in the winter months in these participants (16 between December 1 and February 1, two on April 1). The subjects in this sample were similar to those in the entire study group in age, sex ratio and the proportions resident in the three types of units. Serum was stored at −40°C. At the end of the trial, we measured 25-hydroxy vitamin D [enzyme-linked immunosorbent assay (ELISA), Immunodiagnostic Systems Ltd], parathyroid hormone (ELISA; Diagnostic Systems Laboratories Inc.) and calcium (adjusted for albumin). No blood was taken from control participants.

### Statistical analysis

Relative risk estimates of fractures and falls in the treated group compared with the control group were calculated using a Poisson regression model, which took into account age, sex, the length of time a person was in the trial and the cluster randomisation of the trial. STATA statistical software was used. Based on the number of participants, duration of follow-up and incidence of fractures and falls in the control group, the trial had 80% power to detect a 10% reduction in the incidence of falls in the treated group, 80% power to detect a 45% reduction and 50% power to detect a 34% reduction in the incidence of fractures. The measurements on the serum samples were analysed non-parametrically using Wilcoxon's matched pairs signed ranked test on STATA.

## Results

There were 3,717 participants: 1,762 allocated to the vitamin D group and 1,955 allocated to the control group. The

groups allocated vitamin D and the control group were similar in average age (85 years in each), the proportion who were female (76% in each) and the proportion in different types of accommodation (in the treated group 33, 42 and 25%, and in the control group 36, 42 and 22% were resident in units offering residential, nursing or EMI accommodation, respectively). The mean and median duration in the trial was 10 months (interquartile range 7–14 months). The 3,717 participants were followed for fractures and falls until either the end of the trial, death (347 treated and 322 control) or leaving the care homes to live elsewhere (49 treated and 64 control). During the course of the trial, vitamin D (with or without calcium) was prescribed by GPs to 15 (0.9%) participants allocated vitamin D (in whom the study vitamin D was terminated) and 12 (0.6%) allocated to the control group. No participants were prescribed bisphosphonates or other drugs that increase bone density. Of the 1,762 participants allocated vitamin D, 42 (2%) stopped taking vitamin D before the end of the trial, 28 because of cancer or other serious illness, 13 who refused the tablets and one because hypercalcaemia was diagnosed.

Table 1 shows the numbers of non-vertebral fractures and falls recorded. There was no reduction in the incidence of fractures or falls in the vitamin D-treated group; indeed, the incidence of fractures was directionally higher in the treated group (3.6%) than in the control group (2.6%), but this was not statistically significant. The proportion of participants who had at least one fall was 44% in the vitamin D group and 43% in the control group. The incidence of fractures or falls was no lower in vitamin D-treated than control participants in separate analyses in residents aged under 80 years and 80 and over, and after omitting results from the first 6 or 12 months follow-up.

**Table 1.** Numbers and incidence of all non-vertebral fractures, hip fractures and falls

| | Vitamin D | Control | Relative risk (95% confidence interval) |
|---|---|---|---|
| No. of participants | 1762 | 1955 | |
| All non-vertebral fractures | | | |
| Total number | 66 | 53 | |
| No. (%) of participants who had at least one | 64 (3.6%) | 51 (2.6%) | 1.48 (0.99–2.20) |
| Incidence per 100 person-years | 4.6 | 3.2 | |
| Hip fractures | | | |
| Total number | 24 | 20 | |
| No. (%) of participants who had at least one | 24 (1.3%) | 20 (1.0%) | 1.36 (0.80–2.34) |
| Incidence per 100 person-years | 1.7 | 1.1 | |
| Falls | | | |
| Total number | 2,917 | 3,728 | |
| No. (%) of participants who fell at least once | 770 (44%) | 833 (43%) | 1.09 (0.95–1.25) |
| Incidence per 100 person-years | 201 | 231 | |
| % of participants falling at least once in a given month (on average) | 6.2% | 6.3% | |

**Table 2.** Serum concentration of 25-hydroxy vitamin D, parathyroid hormone, calcium and phosphate (median and 90th centile range) in a sample of 18 residents, showing values immediately before the first dose of vitamin D, 1 month after and 3 months after (i.e. immediately before the second dose of vitamin D)

| | Immediately before first dose | 1 month after first dose | 3 months after first dose |
|---|---|---|---|
| Vitamin D (25-hydroxy vitamin D) (nmol/l) | 47 (35–102) (mean = 59) | 82 (67–185) (mean = 99) | 74 (52–110) (mean = 77) |
| Parathyroid hormone (pmol/l) | 5.1 (1.5–15.8) (mean = 6.2) | 4.7 (1.9–18.8) (mean = 5.7) | 4.4 (2.1–16.0) (mean = 5.6) |
| Calcium[a] (mmol/l) | 2.3 (2.1–2.4) | 2.3 (2.2–2.6) | 2.3 (2.2–2.6) |
| Phosphate (mmol/l) | 1.2 (0.8–1.6) | 1.1 (0.9–1.6) | 1.2 (0.8–1.5) |

[a]Adjusted for serum albumin.

Table 2 shows the results of measurements on blood collected on three occasions in the sample of 18-treated participants from five different homes. The median serum 25-hydroxy vitamin D concentration was 47 nmol/l before the first dose of vitamin D and 82 nmol/l 1 month after, an increase of 31 (21–62) nmol/l [median (5th–95th centile)]. Three months later (immediately before the second dose), the serum concentration was 74 nmol/l, a decrease of only 17 (1–67) nmol/l, confirming previous evidence that 3-monthly dosing is sufficient [22, 23]. There was no change in parathyroid hormone, as expected in view of the relatively high pre-treatment serum 25-hydroxy vitamin D (Table 2) [24]. There were no material changes on average in the serum concentrations of calcium or phosphate, or of protein or liver function tests (not shown).

There was statistically significant variation between units in the incidence of fractures and of reported falls (based on a Poisson regression analysis of the vitamin D and control groups combined, taking age and sex into account). The percentage of residents having one or more fractures in EMI, residential and nursing units was 4.7, 3.5 and 1.9%, respectively, and the proportion having one or more fall was 50, 45 and 37%, respectively. With the type of unit taken into account, however, there was no indication of greater variation between units in the incidence of fractures or falls than would be expected by chance.

## Discussion

Earlier evidence suggested that vitamin D with calcium may prevent hip fracture and other long bone fractures in elderly people living in sheltered housing or residential care [1]. Vitamin D supplementation alone failed to reduce the incidence of fractures or reported falls in our trial, despite the fact that the vitamin D effectively raised the serum 25-hydroxy vitamin D concentration in a representative 1% sample from the treated group. Other trials have shown no

preventive effect of vitamin D with calcium [6–8] or without calcium [8–11] in elderly people living generally in the community; our trial suggests that this is also the case in residential care.

The effect of vitamin D (without calcium) on bone density is known to be modest, increasing it by only ~1% [12, 13]. Our trial suggests that vitamin D similarly has little or no effect in preventing reported falls, confirming the results from smaller trials that vitamin D has little or no protective effect [7, 25]. The absence of a protective effect against hip fracture may therefore not be surprising. The evidence that vitamin D supplementation improves strength and physical performance in elderly people comes from studies of patients either with clinical osteomalacia (serum 25-hydroxy cholecalciferol ~7 nmol/l [14]) or with very low serum 25-hydroxy vitamin D concentration (≤20 nmol/l [15, 16]). Studies in populations like ours with a higher serum 25-hydroxy vitamin D concentration have generally shown little or no effect of additional vitamin D on strength or physical performance [25]. Vitamin D may therefore prevent falls and fractures only in people with very low pre-treatment serum concentration.

Our trial has weaknesses, most notably the non-availability of data on residents who declined to join the trial or who were excluded, such that we cannot exclude selection bias [however, the observation that relative risk estimates directionally favour the control group (Table 1) suggests that our results may still have beeen negative if we could have avoided any selection bias]. Also the sample on whom serum 25-hydroxy vitamin D was measured was small (18 in five homes), although the fact that all the homes provided similar meals and had similar policies on encouraging residents to spend time outdoors may ensure some generalisability of the 1% sample.

In our trial, the median pre-treatment serum vitamin D concentration in the 1% sample was 47 nmol/l (and the mean 59 nmol/l), higher than values previously recorded in institutionalised elderly people [1, 6] and similar to levels observed in free-living elderly people in Northern Europe [4, 24, 26]. The incidences of all non-vertebral fractures (3.2% per year) and of hip fractures (1.1% per year) in the control group are low for elderly people in residential accommodation; they are similar to the incidence previously reported in sheltered accommodation and only about a quarter of that in residential care [17]. The incidence of falls (6.4% of people falling in 1 month, 43% in 10 months) is also lower than that previously reported in residential care (56% of people in 8 months) [20], although a lower incidence may be expected in our study because the falls recorded were limited to those notified by residents to the care home staff (residents did not keep individual fall diaries). Fewer than 1% of residents took calcium/vitamin D separately from the study, so this is not the reason for the high pre-treatment serum levels or the relatively low rates of falls and fractures. It may be that the case mix in these care home residents differed from those previously studied.

The evidence from this trial therefore indicates little or no protective effect of vitamin D against falls and fractures in elderly people living in residential care.

## Key points

- In a randomised trial of vitamin D supplementation in residents of care homes for the elderly, there was no reduction in non-vertebral fractures in treated residents (3.6%) compared with controls (2.6%).
- There was also no reduction in hip fracture (1.3 versus 1.0%).
- There was similarly no reduction in falls (44 versus 43% reported at least one fall).
- The incidence of all fractures (3.2% per year) and hip fractures (1.1% per year) was lower than previously reported in elderly people in residential or nursing care.

## Acknowledgements

We thank Ian Ireland and Clive Bowman of BUPA Care Homes and the staff of the individual care homes for their assistance in launching and maintaining the trial, and Iain MacIntyre and Barry Hoffbrand for help in setting up the trial.

## Source of funding

The study was funded by the Sir Jules Thorn Charitable Foundation.

## References

1. Chapuy MC, Arlot ME, Delmas PD, Meunier PJ. Effect of calcium and cholecalciferol treatment for three years on hip fractures in elderly women. Br Med J 1994; 308: 1081–2.
2. Dawson-Hughes B, Harris SS, Krall EA, Dallal GE. Effect of calcium and vitamin D supplementation on bone density in men and women 65 years of age or older. N Engl J Med 1997; 337: 670–6.
3. Heikinheimo RJ, Inkovaara JA, Harju EJ *et al*. Annual injection of vitamin D and fractures of aged bones. Calcif Tissue Int 1992; 51: 105–10.
4. Trivedi DP, Doll R, Khaw KT. Effect of four monthly oral vitamin $D_3$ (cholecalciferol) supplementation on fractures and mortality in men and women living in the community: randomised double blind controlled trial. Br Med J 2003; 326: 469–72.
5. Komulainen MH, Kröger H, Tuppurainen MT *et al*. HRT and Vit D in prevention of non-vertebral fractures in postmenopausal women; a 5 year randomized trial. Maturitas 1998; 31: 45–54.
6. Chapuy MC, Pamphile R, Paris E *et al*. Combined calcium and vitamin $D_3$ supplementation in elderly women: confirmation of reversal of secondary hyperparathyroidism and hip fracture risk: the Decalyos II Study. Osteoporosis Int 2002; 13: 257–64.
7. Porthouse J, Cockayne S, King C *et al*. Randomised controlled trial of calcium and supplementation with cholecalciferol (vitamin $D_3$) for prevention of fractures in primary care. Br Med J 2005; 330: 1003–8.
8. The RECORD Trial Group. Oral vitamin D3 and calcium for secondary prevention of low-trauma fractures in elderly people (Randomised Evaluation of Calcium Or vitamin D, RECORD): a randomised placebo-controlled trial. Lancet 2005; 365: 1621–8.

9. Lips P, Graafmans WC, Ooms ME, Bezemer D, Bouter LM. Vitamin D supplementation and fracture incidence in elderly persons. Ann Intern Med 1996; 124: 400–6.
10. Meyer H, Smedshaug GB, Kvaavik E, Falch JA, Tverdal A, Pedersen JI. Can vitamin D supplementation reduce the risk of fracture in the elderly? A randomized controlled trial. J Bone Miner Res 2002; 17: 709–15.
11. Smith H, Anderson F, Raphael F, Crozier H, Cooper C. Effect of annual intramuscular vitamin D supplemenation on fracture risk: population-based, randomised, double-blind, placebo-controlled trial. Osteoporosis Int 2004; 15 (Suppl 1): S8.
12. Komulainen M, Tuppurainen MT, Kröger H *et al*. Vitamin D and HRT: no benefit additional to that of HRT alone in prevention of bone loss in early postmenopausal women. A 2.5-year randomized placebo-controlled study. Osteoporosis Int 1997; 7: 126–32.
13. Ooms ME, Roos JC, Bezemer PD, van der Vijgh WJ, Bouter LM, Lips P. Prevention of bone loss by vitamin D supplementation in elderly women: a randomised double-blind trial. J Clin Endocrinol Metab 1995; 80: 1052–8.
14. Glerup H, Mikkelsen K, Poulsen L *et al*. Hypovitaminosis D myopathy without biochemical signs of osteomalacic bone involvement. Calcif Tissue Int 2002; 66: 419–24.
15. Parfitt AM, Gallagher JC, Heaney RP, Johnston CC, Neer R, Whedon GD. Vitamin D and bone health in the elderly. Am J Clin Nutr 1982; 36: 1014–31.
16. Verhaar HJJ, Samson MM, Jansen PAF, de Vreede PL, Manten JW, Duursma SA. Muscle strength, functional mobility and vitamin D in older women. Aging Clin Exp Res 2000; 12: 455–60.
17. Brennan nee Saunders J, Johansen A, Butler J *et al*. Place of residence and risk of fracture in older people: a population-based study of over 65-year-olds in Cardiff. Osteoporosis Int 2003; 14: 515–9.
18. Ooms ME, Vlasman P, Lips P, Nauta J, Bouter LM, Valkenburg HA. The incidence of hip fractures in independent and institutionalized elderly people. Osteoporosis Int 1994; 4: 6–10.
19. Bennett AE, Deane M, Elliott A, Holland WW. Care of old people in residential homes. Br J Prev Soc Med 1968; 22: 193–8.
20. Jensen J, Lundin-Olsson L, Nyberg L, Gustafson Y. Fall and injury prevention in older people living in residential care facilities. A cluster randomized trial. Ann Intern Med 2002; 136: 733–41.
21. McMurdo ME, Millar AM, Daly F. A randomized controlled trial of fall prevention strategies in old peoples' homes. *Gerontology* 2000; 46: 83–7.
22. Weisman Y, Schen RJ, Eisenberg Z *et al*. A single oral high-dose vitamin $D_3$ prophylaxis in the elderly. J Am Geriatr Soc 1986; 34: 515–8.
23. Davies M, Mawer EB, Hann JT, Stephens WP, Taylor JL. Vitamin D prophylaxis in the elderly: a simple effective method suitable for large populations. Age and Ageing 1985; 14: 349–54.
24. Chapuy MC, Preziosi P, Maamer M *et al*. Prevalence of vitamin D insufficiency in an adult normal population. Osteoporosis Int 1997; 7: 439–43.
25. Latham NK, Anderson CS, Reid IR. Effects of vitamin D supplementation on strength, physical performance, and falls in older persons: a systematic review. J Am Geriatr Soc 2003; 51: 1219–26.
26. van der Wielen RPJ, Lőwik MRH, van den Berg H *et al*. Serum vitamin D concentrations among elderly people in Europe. Lancet 1995; 346: 207–10.


Received 6 October 2005; accepted in revised form 6 February 2006