A Higher Dose of Vitamin D Reduces the Risk of Falls in Nursing Home Residents: A Randomized, Multiple-Dose Study

Article *in* Journal of the American Geriatrics Society · March 2007

DOI: 10.1111/j.1532-5415.2007.01048.x · Source: PubMed

CITATIONS
303

READS
117

6 authors, including:

Tai C Chen
Boston University
355 PUBLICATIONS **15,294** CITATIONS
SEE PROFILE

Janice Weinberg
Boston University
118 PUBLICATIONS **2,365** CITATIONS
SEE PROFILE

Michael F Holick
Boston University
808 PUBLICATIONS **62,246** CITATIONS
SEE PROFILE

A Higher Dose of Vitamin D Reduces the Risk of Falls in Nursing Home Residents: A Randomized, Multiple-Dose Study

Kerry E. Broe, MPH, Tai C. Chen, PhD,† Janice Weinberg, ScD,‡ Heike A. Bischoff-Ferrari, MD, MPH,§‖ Michael F. Holick, MD, PhD,† and Douglas P. Kiel, MD, MPH*¶*

OBJECTIVES: To determine the effect of four vitamin D supplement doses on falls risk in elderly nursing home residents.

DESIGN: Secondary data analysis of a previously conducted randomized clinical trial.

SETTING: Seven hundred twenty-five-bed long-term care facility.

PARTICIPANTS: One hundred twenty-four nursing home residents (average age 89).

INTERVENTION: Participants were randomly assigned to receive one of four vitamin D supplement doses (200 IU, 400 IU, 600 IU, or 800 IU) or placebo daily for 5 months.

MEASUREMENTS: Number of fallers and number of falls assessed using facility incident tracking database.

RESULTS: Over the 5-month study period, the proportion of participants with falls was 44% in the placebo group (11/25), 58% (15/26) in the 200 IU group, 60% (15/25) in the 400 IU group, 60% (15/25) in the 600 IU group, and 20% (5/23) in the 800 IU group. Participants in the 800 IU group had a 72% lower adjusted-incidence rate ratio of falls than those taking placebo over the 5 months (rate ratio = 0.28; 95% confidence interval = 0.11–0.75). No significant differences were observed for the adjusted fall rates compared to placebo in any of the other supplement groups.

CONCLUSION: Nursing home residents in the highest vitamin D group (800 IU) had a lower number of fallers and a lower incidence rate of falls over 5 months than those taking lower doses. Adequate vitamin D supplementation in elderly nursing home residents could reduce the number of falls experienced by this high falls risk group. **J Am Geriatr Soc 55:234–239, 2007.**

Key words: vitamin D; falls; nursing home; randomized clinical trial

Elderly nursing home residents have a high risk of falls[1] and fracture[2] and are often deficient in vitamin D.[3–5] In the United States, approximately 1.6 million people lived in nursing homes in 1999, and 46% of these residents were aged 85 and older.[6] Fall-related fracture and injury is a serious problem affecting the quality of life and cost of care for these elderly nursing home residents.[7] Approximately 50% of nursing home residents fall at least once each year,[8] and fall history remains one of the strongest predictors of future falls.[9] Effective interventions to reduce falls are needed in this group at high risk of falling.

Several randomized clinical trials have shown that vitamin D supplementation reduces falls 23% to 53% in residents of nursing homes or residential care,[10,11] and a meta-analysis of vitamin D supplementation and falls (including elderly nursing home participants) found a 22% reduction.[12] Findings for vitamin D supplementation in fracture reduction in nursing home residents have been observed as well.[13] Nevertheless, not all trials with elderly residential care populations have found an association between vitamin D supplements and falls[14] or fracture risk.[15,16] Possible reasons for the observed differences in results across trials in elderly residential care populations include lower doses of vitamin D supplement, healthier populations, and use of calcium supplements.

Although the suggested intake of vitamin D for those aged 70 and older is 600 IU,[17] recommendations have been made to increase the daily requirement,[18] especially in populations known to have low vitamin D status. A meta-analysis (including residential care populations) of vitamin D supplement use and fracture found that 700 to 800 IU are needed for fracture reduction.[19]

To further assess vitamin D supplement use and falls risk in nursing home residents, data from a previously conducted clinical trial were used to compare the effect of four vitamin D supplement doses on the risk of falling with placebo in a group of elderly long-term care residents.

From the *Institute for Aging Research, Hebrew SeniorLife, Boston, Massachusetts; †Vitamin D Laboratory, Department of Medicine, Boston Medical Center, Boston, Massachusetts; ‡Department of Biostatistics, Boston University School of Public Health, Boston, Massachusetts; §Department of Rheumatology and Institute of Physical Medicine and Rehabilitation, University Hospital Zurich, Zurich, Switzerland, ‖Department of Nutrition, Harvard School of Public Health, Boston, Massachusetts; and ¶Division on Aging, Harvard Medical School, Boston, Massachusetts.

Address correspondence to Kerry E. Broe, Institute for Aging Research, Hebrew SeniorLife, 1200 Center Street, Roslindale, MA 02131. E-mail: broe@hrca.harvard.edu

DOI: 10.1111/j.1532-5415.2007.01048.x

0002-8614/07/$15.00

METHODS

Participants

Participants were recruited from the Hebrew Rehabilitation Center for Aged (HRCA), a 725-bed long-term care facility located in Boston, Massachusetts.

To be eligible for the study, residents had to have a life expectancy of 6 months, the ability to swallow medication, and 3 months residency at HRCA. Exclusions included use of glucocorticoids, antiseizure medication, or pharmacological doses of vitamin D; calcium metabolism disorders; severe mobility limitations; or fracture within the previous 6 months. All participants (or legal guardians for participants with moderate to severe cognitive impairment) gave informed consent. The HRCA and Boston University School of Medicine (BU) institutional review boards approved the study protocol.

Study Design and Intervention

This was a 5-month, double-blind, placebo-controlled trial originally designed and powered to compare the effect of four vitamin D doses with placebo on vitamin D status. This original study design was used to compare the effect of the four vitamin D doses with that of placebo on falls over the study period.

Recruitment occurred during an 8-week enrollment period. The HRCA pharmacy randomized participants in blocks of 15 to one of the five study groups (placebo, 200 IU, 400 IU, 600 IU, 800 IU) using a computer-generated randomization list. The pharmacy labeled pill blister packs with names and patient identification numbers only. Blister packs and tablets from all five groups were identical in appearance and taste, so nursing staff, participants, and the study team were unaware of the group assignment.

At study entry, a baseline questionnaire was filled out using chart review assessing participant characteristics. Serum 25-hyrdoxyvitamin D (25(OH)D) measures were obtained at baseline and during the study period.

Nursing staff administered the study pill daily for the 5-month study duration.

The vitamin D_2 tablets were purchased from Tishcon Corporation (Westbury, NY). Vitamin D content of the supplements was verified at the BU Vitamin D Laboratory.[20]

Outcomes

Fall Ascertainment

The primary endpoint was reported number of falls over the study period, ascertained using HRCA's computerized incident-report database, which has been used in previously published falls research.[21,22]

HRCA protocol requires an incident report (indicating date and time) documenting any event not consistent with the routine operation of the facility or the routine care of the resident. A fall is one of the required reporting events and was defined as a sudden, unintentional change in position causing a resident to fall on the ground. Nursing staff fill out the incident report at the time of the event, the primary care physician verifies it, and the information is entered into the incident-report database.

For this analysis, a programmer, not involved with this study and not aware of participant study group assignments, created the falls dataset linking the participant identification number with falls reported during the study period (January to June 1995).

Falls were analyzed according to faller, number of falls, time to first fall, and incident rate ratios of falls.

Compliance

Compliance was calculated as the number of pills taken, as determined according to blister pack counts after the completion of the study divided by the total days a subject was actively participating (alive, living at HRCA, not withdrawn from study).

Additional Measurements

Information on age, sex, weight, height, and multivitamin use was collected using chart review. Body mass index (BMI; kg/m^2) was calculated from height and weight. The number of falls in the previous year was calculated using the HRCA computerized incident-report database. Serum 25(OH)D concentrations were measured at baseline and follow-up using an assay that detected vitamin D_2 and vitamin D_3 to an equivalent extent.[23] Nonfasting venous blood samples (5 mL) were drawn, centrifuged, and stored at $-70^{\circ}C$ before 25(OH)D concentrations were determined. The intra- and interassay variations were 5% and 10%, respectively. The detection limit was 5 ng/mL. Serum 25(OH)D concentrations are presented as ng/mL (1 ng/mL = 1 nmol/L × 0.4). A total vitamin D supplement intake variable was created, totaling the vitamin D from the study pill plus HRCA multivitamin (400 IU, as assayed by the BU laboratory).

Statistical Analysis

Baseline characteristics were compared in each of the five groups using analysis of variance (ANOVA) for continuous variables and chi-square tests for categorical variables. The number of fallers and falls was described over the 5-month period.

Cox proportional hazards regression was used to model time to first fall for each supplement group and compare it with that of placebo. A test for trend for supplement dose was run, adding an ordered variable for each supplement group within the Cox regression model. Based on the pattern of results across the five groups, the risk of falls in the group taking the highest vitamin D dose (800 IU) was compared with the other groups combined. Poisson regression (negative binomial regression to correct for overdispersion)[24] was used to compare the rate of falls in each supplement group with that for the placebo group over the 5-month study period. All analyses were adjusted for age and multivitamin use.

Because not all participants were taking a multivitamin, a secondary analysis was conducted to further assess vitamin D supplement intake using quintiles of total supplement vitamin D intake (study pill + multivitamin use). Baseline characteristics were compared across quintile groups using ANOVA and chi-square tests. Cox proportional hazards regression was used to model time to first fall, adjusted for baseline variables significantly different between quintiles of vitamin D.

All statistical analyses were done using SAS for Windows, version 8.2 (SAS Institute, Inc., Cary, NC).

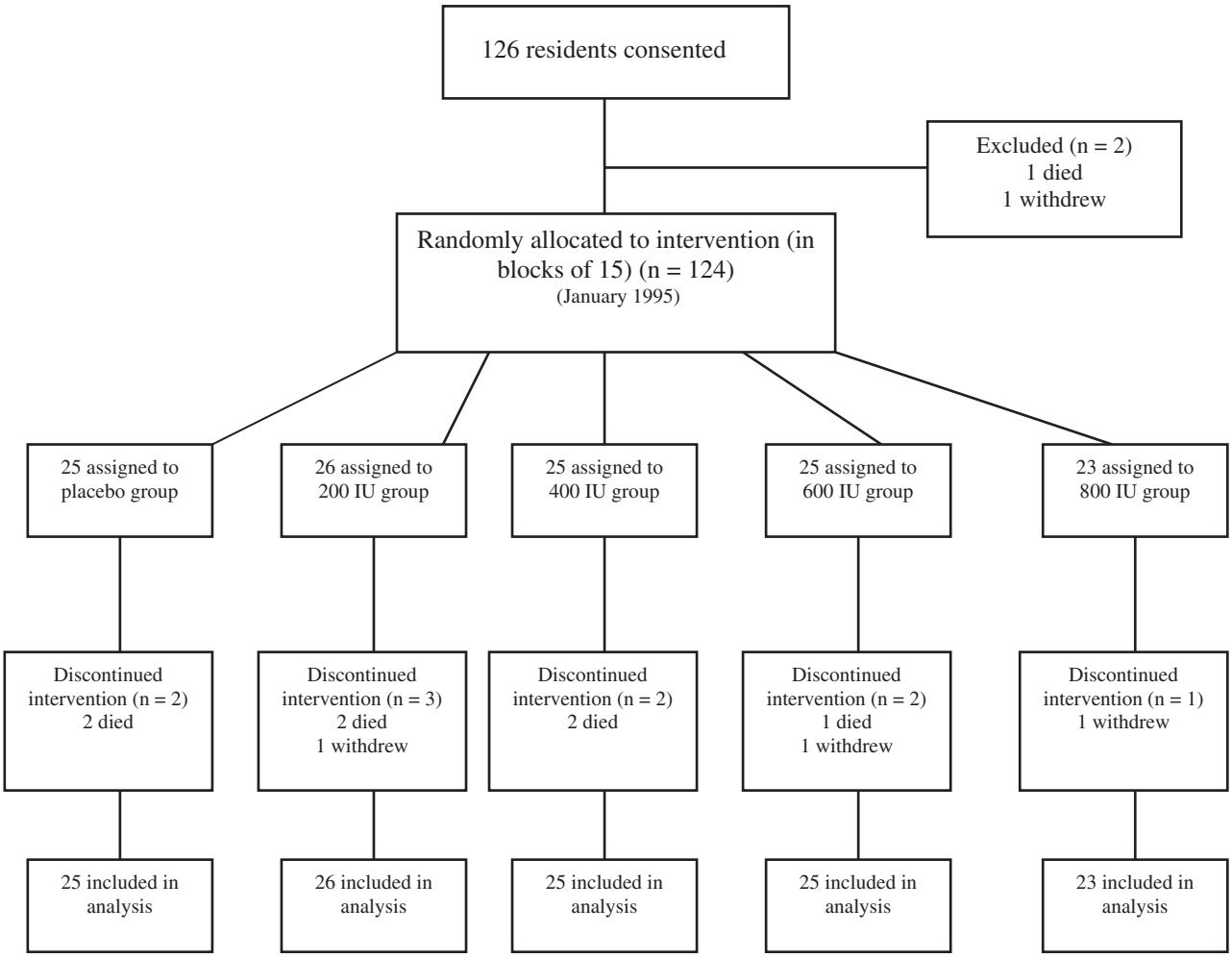

Figure 1. Consort diagram of nursing home participants in the vitamin D supplement trial.

RESULTS

Participant Characteristics

There were 124 residents who took part in the study and were randomly assigned to one of the five groups (Figure 1). Over the 5-month study period, 114 completed the trial. Of the 10 people who did not complete the study, seven died and three withdrew. There were no significant differences between the treatment groups in the number who did not complete the 5-month study with a loss of one to three subjects from each study group (Figure 1).

Average compliance was 97.6%, with only two participants having a compliance level of less than 50%. Compliance did not differ between the study groups.

Baseline Data

Of the 124 participants, 73% were female; mean age ± standard deviation was 89 ± 6 (range 68–104), 63% were taking a daily multivitamin, average serum 25(OH)D was 19.5 ng/mL, and 62% had fallen in the previous year (Table 1). Of those taking a multivitamin at baseline, 54% had low vitamin D concentrations (<20 ng/mL).

As shown in Table 1, no significant differences were observed between the groups for any variable except for age ($P = .005$). Multivitamin use did not significantly differ between the groups.

Follow-Up Data

Distributions of total vitamin D supplement intake were as expected (Table 2), with the placebo group having the lowest intake (272 IU) and the 800 IU group having the highest intake (1,026 IU). Follow-up serum was not available for all participants. For those with valid follow-up 25(OH)D measures (n = 100), the 800 IU group had a mean follow-up concentration of 29.95 ± 5.86 ng/mL, whereas average follow-up serum measures in the other four groups were lower (ranging from 22 to 24 ng/mL). None in the 800 IU group had measures below 20 ng/mL.

Distribution of Falls

Over 5 months, 61 of 124 (59%) participants had at least one fall; 11 of 25 (44%) experienced a fall in the placebo group, 15 of 26 (58%) in the 200 IU group, 15 of 25 (60%) in the 400 IU group, 15 of 25 (60%) in the 600 IU group, and five of 23 (20%) in the 800 IU group (Table 2).

Time to First Fall

Although the number of falls in the 800 IU group was less than half of the placebo group, no significant difference was observed in the risk of falling for participants in the 800 IU and placebo groups, and no linear trend was observed across groups (P-trend = .23) (Table 2). Based upon the

Table 1. Baseline Characteristics of 124 Study Participants According to Vitamin D Supplement Group

Characteristic	Placebo (n = 25)	200 IU (n = 26)	400 IU (n = 25)	600 IU (n = 25)	800 IU (n = 23)	*P*-value	All (n = 124)
Age, mean ± SD	86 ± 7	92 ± 6	88 ± 5	89 ± 6	89 ± 5	.005	89 ± 6
Female, n (%)	20 (80)	19 (73)	18 (72)	17 (68)	16 (70)	.90	90 (73)
Weight, kg, mean ± SD	59.5 ± 13.1	56.9 ± 11.1	63.4 ± 14.5	62.9 ± 16.2	59.0 ± 13.5	.40	60.3 ± 13.8
Height, cm, mean ± SD	153.4 ± 10.7	155.2 ± 11.3	156.7 ± 10.7	155.0 ± 11.3	154.8 ± 12.3	.91	155.0 ± 11.1
Body mass index, kg/m^2, mean ± SD	25.3 ± 5.0	23.7 ± 4.4	25.9 ± 5.2	25.9 ± 5.0	24.5 ± 4.1	.41	25.1 ± 4.8
Multivitamin use, n (%)*	17 (68)	16 (62)	17 (68)	15 (60)	13 (57)	.90	78 (63)
Serum 25(OH)D, ng/mL, mean ± SD†	21.2 ± 11.4	17.8 ± 9.2	20.7 ± 11.6	16.5 ± 7.4	21.4 ± 9.2	.30	19.5 ± 9.9
Low serum 25(OH)D, n (%)‡	12 (50)	17 (65)	12 (48)	17 (71)	10 (48)	.32	68 (57)
Falls in previous year, n (%)	4 (16)	6 (23)	7 (28)	7 (28)	8 (35)		32 (26)
1							
≥2	7 (28)	12 (46)	10 (40)	9 (36)	7 (30)		45 (36)

* 400 IU of vitamin D in multivitamin.
† Four participants had invalid 25-hydoxyvitamin D (25(OH)D) serum concentrations.
‡ <20 ng/mL.
SD = standard deviation.

observation that there was no clear dose response across the supplement groups but a reduction in risk only in the 800 IU group, the risk of falling in the 800 IU group was compared with the other four groups combined, and a 71% lower risk of falling was found (adjusted hazard ratio = 0.29, 95% confidence interval (CI) = 0.11–0.72).

Incidence Rate Ratio

Participants in the 800 IU group had a 72% lower falls incidence rate ratio than participants in the placebo group over the 5 months (Table 2), after adjusting for age and multivitamin use (rate ratio = 0.28, 95% CI = 0.10–0.75). No significant differences were observed between the falls incidence rates of the placebo group and any of the other supplement groups.

Vitamin D Intake Quintiles

As a secondary analysis, total vitamin D supplement intake quintiles were created. Mean intakes ranged from 111 IU in the lowest quintile to 1,093 IU in the highest quintile. The distribution of fallers from lowest to highest quintile was 62% (11/18), 48% (12/25), 54% (14/26), 48% (13/27), and 40% (11/28). Baseline age and BMI were significantly different between the quintiles. Compared with participants in the lowest vitamin D quintile, the age and BMI-adjusted risk of falling was 0.55 (95% CI = 0.24–1.28) in the second quintile, 0.75 (95% CI = 0.34–1.66) in the third quintile, 0.57 (95% CI = 0.25–1.27) in the fourth quintile, and 0.42 (95% CI = 0.18–0.99) in the highest quintile.

DISCUSSION

During this 5-month nursing home study using data from a previously conducted randomized trial, participants in the group taking an 800 IU vitamin D supplement had fewer fallers, fell less, and had a 72% lower falls rate than the placebo group. From early descriptions of muscle weakness in rickets and osteomalacia,[25,26] the importance of vitamin D for muscle function has been recognized and characterized.[25–28] Higher serum 25(OH)D has been associated with better musculoskeletal function,[29,30] leading to a renewed focus on the potential contributions of vitamin D to the risk of falls in older persons.

The findings in the group taking 800 IU are consistent with fall reductions found in a Swiss randomized trial examining residents of long-stay geriatric care over 12 weeks[10] and a large Australian randomized trial examining residents of hostels and nursing homes over 2 years.[11] The Swiss trial found that in 122 elderly women (average age 85) those taking 800 IU of cholecalciferol and 1,200 mg of calcium for 12 weeks had 49% fewer falls than participants taking only 1,200 mg of calcium. The Australian trial found that, in a group of 625 male and female residents (average age 83), the incidence rate ratio for falls was 0.73 (95% CI = 0.57–0.95) in the group supplemented with 10,000 IU of ergocalciferol weekly and 1,000 IU daily for 2 years compared with participants taking placebo. In contrast, a British clinical trial found no association between vitamin D and falls in 3,717 elderly care home residents randomized to 2.5 mg of ergocalciferol every 3 months or placebo for a median follow-up time of 10 months.[14] An overall healthier population in this study, indicated by a low number of

Table 2. Vitamin D Supplement Intake and Fall Outcomes During 5-Month Clinical Trial by Supplement Group for 124 Nursing Home Residents

Outcome	Placebo (n = 25)	200 IU (n = 26)	400 IU (n = 25)	600 IU (n = 25)	800 IU (n = 23)
Total vitamin D supplement intake, IU, mean (range)*	272.00 (0–400)	446.15 (200–600)	672.00 (400–800)	840.00 (600–1,000)	1,026.09 (800–1,200)
Serum 25-hydoxyvitamin D, ng/mL, mean ± SD†	24.12 ± 13.04	24.50 ± 8.29	21.89 ± 9.22	24.47 ± 8.78	29.82 ± 6.26
Faller, n (%)	11 (44)	15 (58)	15 (60)	15 (60)	5 (20)
Total falls, n	31	37	33	41	9
Hazard ratio (95% CI) of time to first fall‡	1.00	1.79 (0.78–3.71)	1.70 (0.77–3.73)	1.68 (0.76–3.71)	0.44 (0.15–1.28)
Incidence rate ratio (95% CI) of falls during the study‡	1.00	1.10 (0.49–2.50)	1.05 (0.48–2.28)	1.21 (0.55–2.61)	0.28 (0.10–0.75)

* Total vitamin D supplement intake = Vitamin D from the study pill + Hebrew Rehabilitation Center for Aged multivitamin (400 IU).
† Valid follow-up serum concentrations available for some participants: placebo (n = 20), 200 IU (n = 22), 400 IU (n = 22), 600 IU (n = 19), 800 IU (n = 17).
‡ Adjusted for age and multivitamin use.
CI = confidence interval.

overall falls, fractures, and higher baseline vitamin D concentrations, could be an explanation as to why no associations were observed.

No "dose response" trend of lower risk of falls with greater supplement dose was observed in this study. The only observed effects were in the group receiving 800 IU. Similar to other nursing home populations,[3–5] participants in this study had low baseline serum 25(OH)D concentrations, with 57% having serum concentrations of less than 20 ng/mL. Of the 78 participants taking a multivitamin at baseline, 54% had vitamin D concentrations less than 20 ng/mL. The standard 400 IU vitamin D supplement found in the HRCA multivitamin did not provide an adequate 25(OH)D concentration for more than half of those taking the multivitamin.

Recently, a panel of vitamin D experts concluded that a minimum serum concentration between 20 and 32 ng/mL would be optimal for bone health, and four of the five experts recommended a minimum concentration between 28 and 32 ng/mL.[18] Valid serum measures at the end of this study were not available for all participants. For the 17 participants in the group taking 800 IU with valid measures, the mean follow-up concentration of 29.95 ng/mL was well within the recommended optimal range, and none had serum measures below 20 ng/mL. Attaining serum concentrations within the recommended optimal range may have positive benefits on muscle function as well as bone health in this elderly nursing home population, and this may be the reason why significant reductions in falling were found only in the group taking 800 IU.

Falls in nursing homes are multifactorial.[31] Ensuring that residents are receiving adequate vitamin D supplementation represents one potential piece of falls intervention programs.

There were several limitations to this study. Multivitamin use was not discontinued for the trial, yet not everyone was taking a multivitamin. This made it difficult to estimate the precise supplement doses within each group. This relationship was further examined by creating quintiles of total vitamin D supplement intake, and it was found that those in the highest intake quintile (average 1,096 IU) had a 58% lower falls risk than those in the lowest intake quintile (111 IU). These results were similar to what was found in the analyses that focused on the randomized groups.

Generalizability of the findings is limited because of the small sample size, participants were all Caucasian, and although participants were on average 89 years old, they were healthier than the other HRCA residents. Because frailer residents may be at greater risk for falls and vitamin D deficiency, replication of these results in a frailer sample of nursing home residents is warranted. In addition, information was not available on how many residents were approached for the study and were excluded. This was a post hoc analysis of a study originally performed to assess serum vitamin D responses. Nevertheless, the randomized, placebo-controlled, multiple-dose study design with high compliance and a well-established computerized incident-report system for fall outcome assessment retained the strengths of the original study. There may have been underreporting of falls, because minor unwitnessed falls would not be reported, yet because of the randomized study design, significant differences in falls underreporting

between the study groups would not be expected. Vitamin D intake from foods or vitamin D repletion through sun exposure was not assessed, but it is likely that both of these sources would be minimal given the diets and activities of most nursing home residents. Furthermore, for participants with information on follow-up serum levels available, the 25(OH)D serum measure reflected total vitamin D, both vitamin D_2 and D_3. Finally, the vitamin D tablet used was D_2 not D_3. Vitamin D_3 potency exceeds that of D_2.[32] Vitamin D_2 was used in this study to be consistent with the type of vitamin D found in HRCA's multivitamin.

In this study cohort, elderly nursing home residents in the highest vitamin D supplement group (800 IU) had a lower rate of falling than those in placebo group or in the lower supplement groups. Ensuring that nursing home residents are receiving adequate daily supplemental vitamin D may reduce the number of falls in elderly nursing home residents and could potentially reduce the risk of fracture in this high-risk group.

ACKNOWLEDGMENTS

We would like to acknowledge the HRCA resident participants and families, nursing staff, and pharmacy department for their contributions to this study; Clorinda Cali for her work in study recruiting and coordination; and Margaret Bryan for her assistance in database creation.

Financial Disclosure: The National Institute on Aging provided funding for this research (P01 AG004390).

Author Contributions: Kerry Broe was involved with study concept, data analysis, and interpretation of data and drafted the manuscript. Tai C. Chen and Michael F. Holick were involved with the original study design, data acquisition, interpretation of data, and manuscript preparation. Janice Weinberg and Heike A. Bischoff-Ferarri assisted with interpretation of data and manuscript preparation. Douglas P. Kiel was involved with study concept and design, acquisition of subjects and data, analysis and interpretation of data, and manuscript preparation.

Sponsor's Role: The sponsor had no role in the design, methods, subject recruitment, data collections, analysis, or preparation of the manuscript.

REFERENCES

1. Rubenstein LZ. Preventing falls in the nursing home. JAMA 1997;278:595–596.
2. Sugarman JR, Connell FA, Hansen A et al. Hip fracture incidence in nursing home residents and community-dwelling older people, Washington State, 1993–1995. J Am Geriatr Soc 2002;50:1638–1643.
3. McMurtry CT, Young SE, Downs RW et al. Mild vitamin D deficiency and secondary hyperparathyroidism in nursing home patients receiving adequate dietary vitamin D. J Am Geriatr Soc 1992;40:343–347.
4. Flicker L, Mead K, MacInnis RJ et al. Serum vitamin D and falls in older women in residential care in Australia. J Am Geriatr Soc 2003;51:1533–1538.
5. O'Dowd KJ, Clemens TL, Kelsey JL et al. Exogenous calciferol (vitamin D) and vitamin D endocrine status among elderly nursing home residents in the New York City area. J Am Geriatr Soc 1993;41:414–421.
6. Jones A. The National Nursing Home Survey, 1999 Summary 2002. Vital Health Stat 13 2002 Jun;(152):1–116.
7. Ray WA, Taylor JA, Brown AK et al. Prevention of fall-related injuries in long-term care: A randomized controlled trial of staff education. Arch Intern Med 2005;165:2293–2298.
8. Tinetti ME. Factors associated with serious injury during falls by ambulatory nursing home residents. J Am Geriatr Soc 1987;35:644–648.
9. Kiely DK, Kiel DP, Burrows AB et al. Identifying nursing home residents at risk for falling. J Am Geriatr Soc 1998;46:551–555.
10. Bischoff HA, Stahelin HB, Dick W et al. Effects of vitamin D and calcium supplementation on falls: A randomized controlled trial. J Bone Miner Res 2003;18:343–351.
11. Flicker L, Macinnis RJ, Stein MS et al. Should older people in residential care receive vitamin D to prevent falls? Results of a randomized trial. J Am Geriatr Soc 2005;53:1881–1888.
12. Bischoff-Ferrari HA, Dawson-Hughes B, Willett WC et al. Effect of vitamin D on falls: A meta-analysis. JAMA 2004;291:1999–2006.
13. Chapuy MC, Arlot ME, Duboeuf F et al. Vitamin D3 and calcium to prevent hip fractures in the elderly women. N Engl J Med 1992;327:1637–1642.
14. Law M, Withers H, Morris J et al. Vitamin D supplementation and the prevention of fractures and falls: Results of a randomised trial in elderly people in residential accommodation. Age Ageing 2006;35:482–486.
15. Meyer HE, Smedshaug GB, Kvaavik E et al. Can vitamin D supplementation reduce the risk of fracture in the elderly? A randomized controlled trial. J Bone Miner Res 2002;17:709–715.
16. Lips P, Graafmans WC, Ooms ME et al. Vitamin D supplementation and fracture incidence in elderly persons. A randomized, placebo-controlled clinical trial. Ann Intern Med 1996;124:400–406.
17. Institute of Medicine. Dietary Reference Intakes: Calcium, Phosphorus, Magnesium, Vitamin D and Fluoride. Washington, DC: National Academy Press, 1999.
18. Dawson-Hughes B, Heaney RP, Holick MF et al. Estimates of optimal vitamin D status. Osteoporos Int 2005;16:713–716.
19. Bischoff-Ferrari HA, Willett WC, Wong JB et al. Fracture prevention with vitamin D supplementation: A meta-analysis of randomized controlled trials. JAMA 2005;293:2257–2264.
20. Chen TC, Turner AK, Holick MF. A method for the determination of the circulating concentration of vitamin D. J Nutr Biochem 1990;1:272–276.
21. Gurwitz JH, Sanchez-Cross MT, Eckler MA et al. The epidemiology of adverse and unexpected events in the long-term care setting. J Am Geriatr Soc 1994;42:33–38.
22. Cali C, Kiel DP. An epidemiologic study of fall-related fractures among institutionalized older people. J Am Geriatr Soc 1995;43:1336–1440.
23. Chen TC, Turner AK, Holick MF. Methods for the determination of the circulating concentration of 25-hydroxyvitamin D. J Nutr Biochem 1990;1:315–319.
24. Lindquist C. How to Estimate Relative Risk in SAS Using PROC GENMOD for Common Outcomes in Cohort Studies [on-line]. Available at www.ats.ucla.edu/STAT/SAS/faq/relative_risk.htm Accessed February 2004.
25. Schott GD, Wills MR. Muscle weakness in osteomalacia. Lancet 1976;1:626–629.
26. Skaria J, Katiyar BC, Srivastava TP et al. Myopathy and neuropathy associated with osteomalacia. Acta Neurol Scand 1975;51:37–58.
27. Smith R, Stern G. Muscular weakness in osteomalacia and hyperparathyroidism. J Neurol 1969;8:511–520.
28. Prineas JW, Mason AS, Henson RA. Myopathy in metabolic bone disease. BMJ 1965;5441:1034–1036.
29. Dhesi JK, Bearne LM, Moniz C et al. Neuromuscular and psychomotor function in elderly subjects who fall and the relationship with vitamin D status. J Bone Miner Res 2002;17:891–897.
30. Bischoff-Ferrari HA, Dietrich T, Orav EJ et al. Higher 25-hydroxyvitamin D concentrations are associated with better lower-extremity function in both active and inactive persons aged >or = 60 y. Am J Clin Nutr 2004;80:752–758.
31. Rubenstein LZ, Josephson KR, Robbins AS. Falls in the nursing home. Ann Intern Med 1994;121:442–451.
32. Armas LA, Hollis BW, Heaney RP. Vitamin D2 is much less effective than vitamin D3 in humans. J Clin Endocrinol Metab 2004;89:5387–5391.