Original Investigation

Exercise and Vitamin D in Fall Prevention Among Older Women
A Randomized Clinical Trial

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IMPORTANCE While vitamin D supplementation and exercise are recommended for prevention of falls for older people, results regarding these 2 factors are contradictory.

OBJECTIVE To determine the effectiveness of targeted exercise training and vitamin D supplementation in reducing falls and injurious falls among older women.

DESIGN, SETTING, AND PARTICIPANTS A 2-year randomized, double-blind, placebo-controlled vitamin D and open exercise trial conducted between April 2010 and March 2013 in Tampere, Finland. Participants were 409 home-dwelling women 70 to 80 years old. The main inclusion criteria were at least 1 fall during the previous year, no use of vitamin D supplements, and no contraindication to exercise.

INTERVENTIONS Four study groups, including placebo without exercise, vitamin D (800 IU/d) without exercise, placebo and exercise, and vitamin D (800 IU/d) and exercise.

MAIN OUTCOMES AND MEASURES The primary outcome was monthly reported falls. Injurious falls and the number of fallers and injured fallers were reported as secondary outcomes. In addition, bone density, physical functioning (muscle strength, balance, and mobility), and vitamin D metabolism were assessed.

RESULTS Intent-to-treat analyses showed that neither vitamin D nor exercise reduced falls. Fall rates per 100 person-years were 118.2, 132.1, 120.7, and 113.1 in the placebo without exercise, vitamin D without exercise, placebo and exercise, and vitamin D and exercise study groups, respectively; however, injurious fall rates were 13.2, 12.9, 6.5, and 5.0, respectively. Hazard ratios for injured fallers were significantly lower among exercisers with vitamin D (0.38; 95% CI, 0.17-0.83) and without vitamin D (0.47; 95% CI, 0.23-0.99). Vitamin D maintained femoral neck bone mineral density and increased tibial trabecular density slightly. However, only exercise improved muscle strength and balance. Vitamin D did not enhance exercise effects on physical functioning.

CONCLUSIONS AND RELEVANCE The rate of injurious falls and injured fallers more than halved with strength and balance training in home-dwelling older women, while neither exercise nor vitamin D affected the rate of falls. Exercise improved physical functioning. Future research is needed to determine the role of vitamin D in the enhancement of strength, balance, and mobility.

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Invited Commentary

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Falls are the leading cause of unintentional injuries and fractures in older adults. Although less than 1 in 10 falls results in a fracture, approximately 20% of falls lead to injury requiring medical attention.[1] Therefore, fall prevention is widely considered the most essential element in injury and fracture prevention programs in elderly populations.[2,3] There is strong high-quality evidence from randomized clinical trials and subsequent systematic reviews and meta-analyses that regular strength and balance training can reduce the risk of falling in community-dwelling older adults by 15% to 50%.[4,5]

Vitamin D, in turn, is known to be vital for bone metabolism and health. Insufficient serum 25-hydroxyvitamin D (25[OH]D) levels are associated with increased bone loss and risk of fractures as well as increased fall rates. Furthermore, it has been suggested that those with low 25(OH)D levels have lower physical performance and greater declines in physical functioning.[6,7] However, systematic reviews and meta-analyses of clinical trials exploring the role of vitamin D in reducing falls and fractures in community-dwelling older people and in improving physical functioning are inconclusive.[8-11]

The aim of this study was to investigate the separate and combined effects of multimodal exercise training and vitamin D supplementation in reducing falls and injurious falls and fallers as well as to assess their effects in improving bone density and physical functioning among older women at risk for falling.

Methods

Trial Design

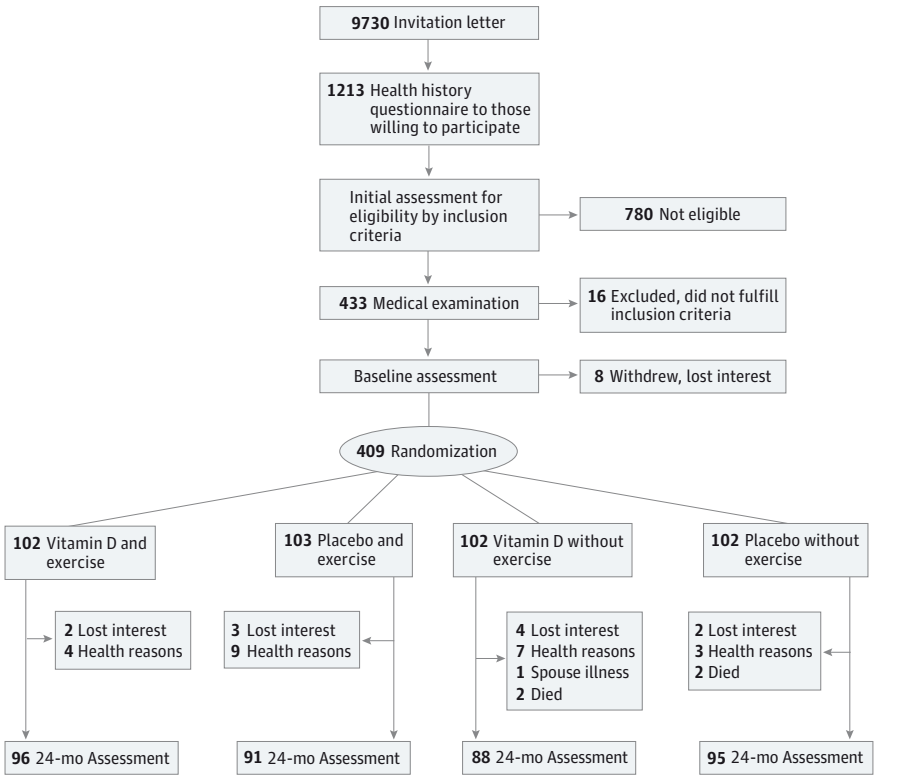
This study was a 2-year, double-blind, placebo-controlled vitamin D and open exercise intervention trial with 4 arms (**Figure 1**). The trial was performed between April 2010 and March 2013. Eligibility criteria and recruitment of participants have been described in detail previously.[12] Briefly, home-dwelling women 70 to 80 years old living in Tampere, Finland, were eligible if they had fallen at least once during the previous 12 months, did not use vitamin D supplements, and had no contraindications to exercise. Individuals who participated in moderate to vigorous exercise more than 2 hours per week were excluded from the study.

The study protocol was approved by the ethics committee of the Tampere University Hospital, Tampere, Finland (approval R09090). The study protocol can be found in the trial protocol in Supplement 1. Each participant provided written informed consent before randomization. The study protocol is registered at clinicaltrials.gov (identifier NCT00986466).

Setting and Participants

In total, 409 participants were randomly assigned to 1 of 4 groups using a computer-generated list based on simple randomization with random allocation sequence to ensure equal group sizes. The groups were (1) placebo without exercise,

Figure 1. CONSORT Diagram



CONSORT indicates Consolidated Standards of Reporting Trials.

(2) vitamin D (800 IU/d) without exercise, (3) placebo and exercise, and (4) vitamin D (800 IU/d) and exercise.

Participants received one daily pill containing 800 IU (20 μg) of vitamin D_3 or placebo for 24 months (trial protocol in Supplement 1).[12] All tablets were provided by Oy Verman Ab (Kerava, Finland) and were similar in size, appearance, and taste. Each participant received a pack of pills for 6 months at a time. Used packs were returned at the time of laboratory measurements every 6 months, and new full packs were given. The compliance was confirmed by pill counts.

Exercise consisted of supervised, progressive group training classes 2 times a week for the first 12 months and once a week for the remaining 12 months of the 24-month intervention (trial protocol in Supplement 1).[12] Training periods alternating between exercise hall and gym classes were led by physiotherapists (R.P. and S.K.), who also monitored attendance. Exercise hall classes focused on balance challenging, weight bearing, strengthening, agility, and functional exercises. Gym classes included a combination of pin-loaded weight machines, pulleys, and free weights, beginning with 30% to 60% of one repetition maximum and progressing to a target level of 60% to 75% of one repetition maximum. Exercise intensity was estimated in metabolic equivalent tasks (METs) every 8 weeks (version 3.0.1.0; Firstbeat Technologies). The exercisers also had a home-training program (5-15 minutes), modified from the supervised exercises, to be performed on all rest days. The nonexercising groups were asked to maintain their prestudy level of physical activity.

Outcome Measures

The primary outcome was monthly reported falls. Secondary outcomes included injurious falls, the number of fallers and injured fallers, bone density, and physical functioning (muscle strength, balance, and mobility).

The number of falls was obtained from prospective fall diaries returned monthly via mail, and details of each registered fall were ascertained by a telephone call. A *fall* was defined as "an unexpected event in which the participant comes to rest on the ground, floor or lower level."[13(p1619)] Injurious falls were those for which participants sought medical care (nurse, physician, or hospital) and included injuries such as bruises, abrasions, contusions, sprains, fractures, and head injuries. Less injurious falls for which medical treatment was not sought were not included in the analysis.

Data Collection

All measurements were obtained at baseline, 12 months, and 24 months. Blood samples and physical functioning were also assessed at 6 months and 18 months. Assessors were blinded to group assignments.

Body height and weight were measured with standard methods. Dietary intake of calcium and vitamin D was assessed with a validated food frequency questionnaire.[14]

Body composition and areal bone mineral density (BMD) of the lumbar spine and left proximal femur were assessed using dual-energy x-ray absorptiometry (Lunar Prodigy Advance; GE Healthcare).[15] Distal site (5%) and the mid-diaphysis (50%) of the tibia were assessed with peripheral quantitative computed tomography (XCT 3000; Norland/Stratec).[16]

Physical functioning was assessed by the Short Physical Performance Battery,[17] which comprised static balance, 4-m normal walking speed, and 5-time chair stand tests and by the Timed Up and Go (TUG) test.[18] Dynamic balance was assessed using backward walking.[19] Maximal isometric leg extensor strength at a knee angle of 110° was measured by a strain gauge dynamometer (custom made; Tamtron). Each participant recorded her daily steps with a pedometer (HJ-112-E; Omron) over the entire 24-month study period. All tests are regularly used in our laboratory and have good reproducibility.

Analysis of 25(OH)D and Parathyroid Hormone Levels

Fasting serum 25(OH)D level was measured as a marker of vitamin D metabolism with an immunoenzymometric assay (Octeia; IDS). Reproducibility was ensured by adhering to the Vitamin D External Quality Assessment Scheme (DEQAS; http://deqas.kpmd.co.uk). The laboratory received the DEQAS proficiency certificate in 2012. Interassay variation was avoided by measuring all samples from the same individuals in the same series. Serum intact parathyroid hormone was measured with an automated immunoassay (Immuliate 1000; Siemens Healthcare Diagnostics).

Randomization and Blinding

The participants were enrolled by the corresponding author. The study statistician (K.T.) generated the participant list using validated randomization software. He was blinded to the study participants and their characteristics and randomly allocated them into 4 groups (simple randomization). The participants and study personnel were blinded to the vitamin D treatment group assignments. The randomization codes were opened after the data collection was completed and checked.

Statistical Analysis

Power calculations indicated that a sample size of 260 (130 exercisers and 130 nonexercisers) would have an 80% power to detect a 30% between-group difference in the rate of falls during the 2-year intervention with a significance level of $\alpha = .05$. However, to eliminate the role of chance in detecting the possible interaction of vitamin D and exercise, 400 participants (100 in each group) were recruited into the study.

All data were analyzed on an intent-to-treat basis. Follow-up times for falls, fallers and injurious falls, and injured fallers were calculated from the beginning to the end of the 24-month intervention unless the participant withdrew from the study or died. Pairwise multiple comparisons with Sidak adjustment were first used to test the differences among treatment groups and interaction between vitamin D and exercise. Sidak adjustment enables the simultaneous pairwise comparison of multiple groups.

Fall incidence rates were calculated as the total number of falls divided by the time over which falls were monitored (100 person-years) in each group. Negative binomial regression was used to estimate the incidence rate ratios for falls and

Table 1. Baseline Characteristics of the Study Groups[a]

Characteristic	Placebo Without Exercise (n = 102)	Vitamin D Without Exercise (n = 102)	Placebo and Exercise (n = 103)	Vitamin D and Exercise (n = 102)
Age, y	73.8 (3.1)	74.1 (3.0)	74.8 (2.9)	74.1 (2.9)
Height, cm	160.7 (5.4)	159.2 (5.8)	159.4 (6.1)	159.7 (5.9)
Weight, kg	72.0 (12.4)	73.0 (13.1)	70.9 (10.6)	73.2 (10.5)
Fat, %	41.1 (6.7)	42.0 (7.2)	41.3 (6.4)	42.8 (5.3)
Calcium intake, mg/d	1040 (345)	1125 (420)	1119 (346)	1109 (385)
Vitamin D intake, µg/d	10.2 (4.1)	10.9 (4.2)	10.3 (3.6)	10.4 (3.9)
Serum 25-hydroxyvitamin D level, ng/mL	27.1 (7.5)	26.4 (6.9)	27.8 (7.2)	26.2 (7.0)
Serum parathyroid hormone level, pg/mL	5.0 (2.7)	5.0 (2.2)	4.7 (2.0)	5.2 (2)
Fasting serum calcium level, mg/dL	9.40 (0.76)	9.40 (0.76)	9.36 (0.76)	9.40 (0.80)
Fasting serum phosphorus level, mg/dL	3.22 (0.49)	3.31 (0.46)	3.22 (0.46)	3.19 (0.49)
Daily steps during first month	6000 (2636)	5812 (2842)	5920 (2458)	5831 (2504)
Mini-Mental State Examination score (range of 0-30)[b]	28.5 (1.7)	28.3 (1.4)	28.2 (1.4)	28.3 (1.5)
Short Physical Performance Battery score, mean (range)	10.6 (3-12)	10.7 (1-12)	10.9 (7-12)	10.8 (5-12)
Activities of Daily Living score (range of 6-36)[c]	6.7 (1.6)	7.0 (2.2)	6.8 (1.9)	6.9 (1.8)
Instrumental Activities of Daily Living score (range of 8-48)[c]	9.8 (2.7)	10.7 (4.9)	9.9 (3.8)	10.3 (4.0)
Mobility difficulties outdoors, No. (%)	18 (17.6)	19 (18.6)	17 (16.5)	17 (16.7)
No. of children	2.0 (1.3)	2.0 (1.2)	2.1 (1.3)	2.1 (1.2)
Age at menopause, y	50 (5)	49 (5)	49 (5)	50 (5)
Use of hormone therapy, No.				
Never	41	45	40	38
Ever	38	38	46	44
Current	23	19	17	20
Medical conditions, No.				
Hypertension	42	52	36	53
Cardiovascular disease	18	16	21	16
Hypothyroidism	19	17	25	27
Diabetes mellitus	9	12	10	6
Osteoarthritis	23	29	26	34
Depression	2	5	2	5
None	16	10	19	8
No. of medications	2.5 (2.0)	2.6 (1.9)	2.3 (2.0)	2.7 (1.9)
Blood pressure, mm Hg				
Systolic	146 (17)	148 (18)	148 (14)	148 (17)
Diastolic	81 (9)	82 (10)	82 (9)	81 (8)

SI conversion factors: To convert serum 25-hydroxyvitamin D level to nanomoles per liter, multiply by 2.496; to convert serum parathyroid hormone level to nanograms per liter, multiply by 1.0; to convert fasting serum calcium level to millimoles per liter, multiply by 0.25; and to convert fasting serum phosphorus level to millimoles per liter, multiply by 0.323.

[a] Values are mean (SD) unless otherwise indicated.

[b] Higher score indicates better functioning.

[c] Lower score indicates better functioning.

injurious falls. Cox proportional hazards regression models were used to calculate hazard ratios for fallers and injured fallers in each group, with the placebo without exercise group as the reference.

For physical functioning and bone traits, between-group differences in time were estimated by linear mixed models for normally distributed outcomes and by generalized linear mixed models with gamma distribution and log link function for nonnormally distributed outcomes using age, height, weight, and the use of hormone therapy as covariates. These methods allowed the incorporation of incomplete longitudinal data into the analysis. All statistical analyses were conducted using a software program (SPSS, version 22; IBM).

Results

There were no clinically relevant between-group differences in age or anthropometry at baseline (**Table 1**). Body composition did not change significantly during the trial. The mean (SD) daily dietary calcium intake was sufficient at 1098 (378) mg at baseline and 1212 (400) mg at 24 months. The mean (SD) daily dietary vitamin D intake was 10.4 (3.9) µg at baseline and 10.5 (4.3) µg at the end of the intervention. Alcohol consumption was low, and 13 women were current smokers. Fifty-three women (13.0%) were taking no medication, while 87.0% had at least 1 diagnosed chronic disease, most commonly cardiovascular.

Table 2. Rate of Falls per 100 Person-years in Each Study Group During the 24-Month Intervention and IRR for Falls and Injurious Falls

Outcome	Placebo Without Exercise	Vitamin D Without Exercise	Placebo and Exercise	Vitamin D and Exercise
All falls	118.2	132.1	120.7	113.1
Injurious falls	13.2	12.9	6.5	5.0
IRR (95% CI)				
All falls	1 [Reference]	1.08 (0.78-1.52)	1.07 (0.77-1.45)	0.99 (0.72-1.39)
Injurious falls	1 [Reference]	0.84 (0.45-1.57)	0.46 (0.22-0.95)	0.38 (0.17-0.81)
All multiple falls	1 [Reference]	1.05 (0.60-1.86)	1.11 (0.63-1.94)	1.14 (0.65-1.99)
Multiple injurious falls	1 [Reference]	1.04 (0.56-1.96)	1.10 (0.59-2.05)	1.54 (0.84-2.81)

Abbreviation: IRR, incidence rate ratio.

Thirty-nine women (9.5%) did not complete the end point measurements, with most citing health reasons, and 4 women died (Figure 1). The mean pill compliance was 98.1% (range, 42.6%-100%), while the mean exercise compliance (measured as attendance at all offered training sessions for group and home training) was 72.8% (range, 0%-97.4%) and 66.1% (0%-100%), respectively. The mean intensity of supervised training ranged from 1.6 METs (stretching or resting) to 5.6 METs. Individual maximal values were more than 7 METs.

In general, the training program was well tolerated. There were no severe adverse effects or injuries due to the training. Twenty-two participants from the exercise groups and 1 participant from the nonexercise groups consulted the attending physician (P.K.) because of musculoskeletal complaints, mainly mild overuse symptoms (eTable in Supplement 2). In addition, 3 injuries occurred during the gym training. Three exercisers withdrew from training during the first weeks of the program because of preexisting osteoarthritic symptoms.

Vitamin D levels differed significantly between the vitamin D and placebo groups. The mean (SD) serum 25(OH)D levels remained stable in the placebo groups at 27.5 (7.4) ng/mL at baseline and 27.5 (6.9) ng/mL at 24 months, with small seasonal variation, while the mean (SD) levels increased in the vitamin D groups from 25.1 (6.9) ng/mL at baseline to 37.0 (7.4) ng/mL at 24 months (eFigure 1 in Supplement 2) (to convert serum 25[OH]D level to nanomoles per liter, multiply by 2.496). Small seasonal variations were observed in serum intact parathyroid hormone in the placebo groups, while that in the vitamin D groups declined slightly from baseline, remaining stable thereafter.

No interaction was found between vitamin D and exercise. In total, there were 928 falls and 281 fallers, with no between-group differences (the rate of falls is summarized in **Table 2**). However, hazard ratios for injured fallers were lower in both exercise groups compared with the placebo without exercise group. Hazard ratios were 0.47 (95% CI, 0.23-0.99) for the placebo and exercise group and 0.38 (95% CI, 0.17-0.83) for the vitamin D and exercise group. The vitamin D without exercise group did not differ from the placebo without exercise group (**Figure 2**). Results were similar for the incidence rate ratios of injurious falls (Table 2). The numbers of multiple fallers (n = 190) and multiple injured fallers (n = 117) were distributed similarly across the groups.

During the intervention, femoral neck BMD declined in all groups, but the mean decline was greatest in the placebo without exercise group and differed significantly from that in all other study groups (**Table 3**). Lumbar spine BMD did not change significantly in any group. Vitamin D increased trabecular bone density at the tibia slightly but significantly between the vitamin D and exercise group and the placebo without exercise group ($P = .02$).

The mean (SD) number of daily steps was 5930 (2512) over the entire study period, with no between-group differences. Individual daily steps ranged from 1200 to 16 500.

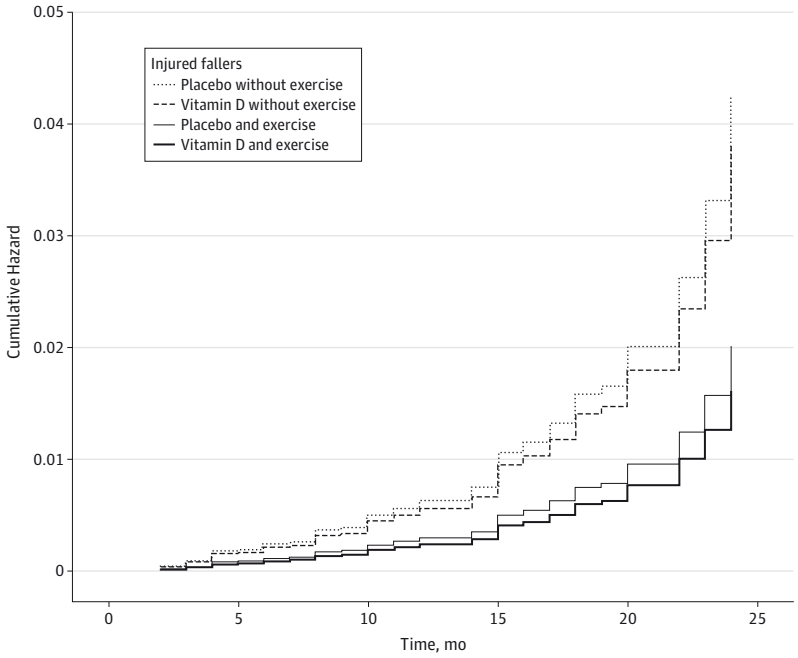
Changes in physical functioning are summarized in Table 3 and eFigure 2 in Supplement 2. Normal walking speed was maintained in the placebo and exercise group compared with the placebo without exercise group ($P = .007$), while declining similarly in other groups. Chair stand time improved in both exercise groups, showing more than 6% improvement compared with the placebo without exercise group but reaching statistical significance only in the placebo and exercise group ($P = .03$). The TUG time deteriorated significantly more in the vitamin D without exercise group compared with the placebo without exercise group ($P = .01$). Other groups did not differ from the placebo without exercise group. Backward walking improved significantly among exercisers. The difference compared with the placebo without exercise group was statistically significant in the placebo and exercise group ($P = .001$) and in the vitamin D and exercise group ($P = .03$). Irrespective of vitamin D, exercise increased muscle strength, while vitamin D alone had no effect. The predicted mean increase in lower limb extension strength was almost 15% in both exercise groups and differed significantly from the placebo without exercise group ($P < .001$).

Discussion

This large randomized clinical trial of vitamin D and exercise showed that exercise training reduced injurious falls among home-dwelling older women, while the rate of falls was not affected by either treatment. Exercise improved physical functioning but vitamin D did not (contrary to initial expectations). However, vitamin D reduced bone loss at the femoral neck and increased trabecular density at the distal tibia.

Current evidence for the effectiveness of vitamin D in fall prevention is inconsistent, most likely because of varying study designs and baseline 25(OH)D levels as well as different dos-

Figure 2. Hazard Ratios (95% CIs) for Fallers, Injured Fallers, and Multiple Fallers Using the Placebo Without Exercise Group as the Reference



	Vitamin D Without Exercise	Placebo and Exercise	Vitamin D and Exercise
Fallers	0.77 (0.54-1.11)	0.93 (0.66-1.31)	0.91 (0.64-1.28)
Injured fallers	0.89 (0.47-1.69)	0.47 (0.23-0.99)[a]	0.38 (0.17-0.83)[a]
Multiple fallers	1.07 (0.71-1.62)	1.14 (0.76-1.71)	1.14 (0.77-1.71)

Cumulative hazard is presented for the injured fallers.
[a]$P < .05$ compared with the placebo without exercise group.

ages or types of vitamin D supplements used. According to some experts, an adequate serum 25(OH)D level should be at least 30 ng/mL,[20,21] while many guidelines consider 20 ng/mL to be sufficient.[22] We aimed to recruit participants from the general population regardless of vitamin D status, and serum 25 (OH)D levels were measured only after randomization.

There is also inconclusive evidence on whether vitamin D could modulate physical functioning.[4,8] In a population-based survey of men and women 60 years or older, a higher 25(OH)D level was associated with better neuromuscular function.[7] Surprisingly, chair stand test performance appeared to decline at the highest 25(OH)D levels exceeding 120 nmol/L (>48 ng/mL),[7] possibly because of few observations in the highest category. This finding needs confirmation. In trials using high dosages of vitamin D, high 25(OH)D levels have increased the risk of falls and fractures, suggesting negative influences on balance and mobility.[23,24] Little is known about the combined effects of vitamin D and exercise. Results of 2 pilot studies[25,26] have suggested a positive influence. In frail elderly patients with acute hip fracture, Bischoff-Ferrari et al[9] reported that vitamin D treatment reduced hospital readmission but not falls, whereas physiotherapy was successful in reducing falls but not hospital readmission. An effect on falls was found in the physical therapy group, although gains in physical functioning were found only among participants adherent to the physiotherapy home program.

In the present trial, exercise training (irrespective of vitamin D supplementation) reduced injurious falls and decreased the number of injured fallers. Apparently, this effect was attributable to improved physical functioning. Muscle strength and balance training has been shown to prevent falls in community-dwelling older adults, and recent meta-analyses have confirmed that such exercise programs are effective in preventing fall-induced injuries.[3,27]

Exercise improved muscle strength, balance, and mobility except for the TUG time. Surprisingly, vitamin D seemed to worsen the TUG time. Similarly, although normal walking speed was maintained in both exercise groups with or without vitamin D, the vitamin D without exercise group showed the greatest decline. Another unexpected finding was that exercisers treated with vitamin D supplementation showed consistently smaller benefits than exercisers receiving placebo. Therefore, our results indicate that vitamin D may not improve neuromuscular function, at least when vitamin D intake is sufficient.

Despite improved physical performance, exercise conferred no effect on the overall fall rate. Recent studies[28,29] have provided similar results. More falls have been reported among exercisers despite improved muscle strength and physical performance.[28] Nevertheless, in our study, the rate of injurious falls and injured fallers more than halved among exercisers. Good physical condition may help prevent injuries during a fall, perhaps via better and safer landing techniques. This trend fully concurs with recent meta-analyses.[3,27]

Exercise training was primarily intended to improve balance, muscle strength, and mobility rather than bone density

Table 3. Baseline Values in Bone Traits and Physical Functioning in Each Study Group

Outcome	Absolute Value, Mean (SD)	Mean (95% CI), %		*P* Value[a]
		Change at 12 mo	Change at 24 mo	
Femoral Neck BMD, g/cm^2				
Placebo without exercise	0.87 (0.14)	−1.25 (−4.78 to 2.41)	−1.22 (−4.75 to 2.45)	NA
Vitamin D without exercise	0.82 (0.11)	−0.30 (−3.92 to 3.46)	−0.87 (−4.47 to 2.86)	.02
Placebo and exercise	0.85 (0.12)	−0.32 (−3.90 to 3.39)	−0.98 (−4.55 to 2.73)	.01
Vitamin D and exercise	0.88 (0.13)	−0.51 (−4.03 to 3.14)	−1.24 (−4.72 to 2.38)	.04
Lumbar Spine BMD, g/cm^2				
Placebo without exercise	1.15 (0.23)	0.62 (−3.66 to 4.90)	1.21 (−3.09 to 5.51)	NA
Vitamin D without exercise	1.12 (0.20)	0.60 (−3.83 to 5.03)	1.29 (−3.16 to 5.75)	.33
Placebo and exercise	1.13 (0.21)	0.12 (−4.24 to 4.48)	0.48 (−3.91 to 4.87)	.32
Vitamin D and exercise	1.17 (0.22)	0.33 (−3.87 to 4.53)	0.77 (−3.43 to 4.97)	.77
Distal Tibia Trabecular Density, mg/cm^3				
Placebo without exercise	220.3 (34.8)	−0.25 (−3.54 to 3.03)	−0.49 (−3.77 to 2.80)	NA
Vitamin D without exercise	217.9 (28.6)	−0.09 (−3.50 to 3.32)	0.03 (−3.36 to 3.42)	.12
Placebo and exercise	224.5 (29.4)	−0.13 (−3.39 to 3.13)	−0.16 (−3.43 to 3.11)	.41
Vitamin D and exercise	224.4 (31.4)	0.17 (−3.05 to 3.39)	0.19 (−3.04 to 3.42)	.02
Tibial Shaft Cortical Density, mg/cm^3				
Placebo without exercise	1104.6 (37.0)	−0.07 (−0.78 to 0.64)	−0.13 (−0.85 to 0.58)	NA
Vitamin D without exercise	1106.3 (38.0)	0.05 (−0.65 to 0.75)	0.11 (−0.60 to 0.82)	.08
Placebo and exercise	1106.5 (33.6)	−0.04 (−0.72 to 0.65)	−0.08 (−0.77 to 0.62)	.68
Vitamin D and exercise	1114.4 (34.0)	−0.06 (−0.75 to 0.63)	−0.12 (−0.82 to 0.58)	.93
Tibial Shaft Cortical Area, mm^2				
Placebo without exercise	277.7 (40.5)	−0.12 (−3.29 to 3.05)	−0.24 (−3.44 to 2.95)	NA
Vitamin D without exercise	273.5 (39.7)	−0.31 (−3.62 to 3.01)	−0.86 (−4.20 to 2.49)	.55
Placebo and exercise	277.5 (36.6)	−0.36 (−3.60 to 2.88)	−1.16 (−4.42 to 2.10)	.33
Vitamin D and exercise	271.9 (31.3)	−0.70 (−3.89 to 2.50)	−1.27 (−4.44 to 1.91)	.64
Tibial Shaft Strength Strain Index, mm^3				
Placebo without exercise	1749.3 (270.7)	0.22 (−3.34 to 3.79)	0.25 (−3.34 to 3.84)	NA
Vitamin D without exercise	1696.5 (283.7)	0.06 (−3.71 to 3.84)	−0.31 (−4.13 to 3.50)	.25
Placebo and exercise	1716.6 (277.0)	−0.17 (−3.80 to 3.46)	−1.16 (−4.82 to 2.50)	.21
Vitamin D and exercise	1719.0 (248.7)	−0.74 (−4.32 to 2.85)	−1.26 (−4.83 to 2.31)	.40
Ratio of Cortical to Total Area				
Placebo without exercise	0.17 (0.05)	−1.44 (−9.16 to 6.28)	−2.00 (−9.76 to 5.77)	NA
Vitamin D without exercise	0.16 (0.05)	−0.65 (−8.58 to 7.29)	−1.12 (−9.13 to 6.89)	.48
Placebo and exercise	0.17 (0.05)	−0.78 (−8.49 to 6.93)	−0.07 (−7.83 to 7.70)	.17
Vitamin D and exercise	0.18 (0.06)	−0.77 (−7.98 to 6.44)	−1.66 (−8.83 to 5.50)	.98
Normal Walking Speed, m/s				
Placebo without exercise	1.04 (0.21)	−1.64 (−5.65 to 2.36)	−2.51 (−6.72 to 1.69)	NA
Vitamin D without exercise	1.00 (0.21)	−2.73 (−7.03 to 1.58)	−3.30 (−7.82 to 1.22)	.72
Placebo and exercise	1.01 (0.19)	4.21 (0.05 to 8.36)	−0.10 (−4.51 to 4.30)	.007
Vitamin D and exercise	1.03 (0.20)	0.03 (−3.98 to 4.03)	−1.80 (−6.00 to 2.41)	.46
Chair Stand Time, s				
Placebo without exercise	12.6 (2.4)	−0.76 (−5.07 to 3.76)	−1.30 (−6.02 to 3.65)	NA
Vitamin D without exercise	12.6 (3.3)	−1.57 (−5.97 to 3.04)	−3.49 (−8.25 to 1.52)	.46
Placebo and exercise	12.5 (2.8)	−4.30 (−8.39 to −0.06)	−7.80 (−12.20 to −3.20)	.03
Vitamin D and exercise	12.4 (2.5)	−3.63 (−7.70 to 0.63)	−6.95 (−11.30 to −2.40)	.05
Timed Up and Go Time, s				
Placebo without exercise	9.3 (2.1)	−0.79 (−5.36 to 4.01)	−1.93 (−6.70 to 3.09)	NA
Vitamin D without exercise	9.7 (6.4)	2.25 (−2.68 to 7.44)	4.20 (−1.10 to 9.79)	.01
Placebo and exercise	8.9 (1.9)	−0.19 (−5.46 to 5.37)	0.35 (−5.26 to 6.28)	.19
Vitamin D and exercise	8.9 (1.6)	−0.99 (−6.05 to 4.36)	−1.75 (−7.11 to 3.93)	.63

(continued)

Table 3. Baseline Values in Bone Traits and Physical Functioning in Each Study Group (continued)

Outcome	Absolute Value, Mean (SD)	Mean (95% CI), %		*P* Value[a]
		Change at 12 mo	Change at 24 mo	
Backward Walking, Proportion of Those Able to Do 6.1 min, %				
Placebo without exercise	41.8	4.41 (−5.19 to 14.42)	7.76 (−2.87 to 18.47)	NA
Vitamin D without exercise	30.3	2.91 (−5.89 to 12.87)	9.48 (−0.66 to 20.08)	.68
Placebo and exercise	45.8	30.92 (21.87 to 38.09)	26.27 (15.71 to 35.13)	.001
Vitamin D and exercise	51.0	24.57 (15.63 to 31.98)	25.47 (15.30 to 33.39)	.03
Muscle Strength, N/kg				
Placebo without exercise	23.1 (6.1)	2.8 (−3.4 to 9.0)	1.8 (−4.8 to 8.4)	NA
Vitamin D without exercise	23.4 (7.7)	−0.9 (−7.1 to 5.4)	1.5 (−5.0 to 8.1)	.10
Placebo and exercise	23.6 (6.0)	17.3 (11.4 to 23.2)	14.0 (7.8 to 20.2)	<.001
Vitamin D and exercise	22.2 (6.6)	18.0 (11.7 to 24.1)	15.6 (9.1 to 22.2)	<.001

Abbreviations: BMD, bone mineral density; NA, not applicable.

[a] Compared with the placebo without exercise group.

because limited physical capacity or comorbidities of participants were likely to restrict the intensity or type of loading needed to strengthen bone. Nevertheless, both vitamin D groups showed increased trabecular bone density in the tibia, suggesting that the mean 25(OH)D levels were sufficient for a skeletal effect (84.6% of participants in both vitamin D groups exceeded the target level of ≥30 ng/mL).[20] Although vitamin D and exercise (alone or in combination) could not increase femoral neck BMD, both treatments reduced bone loss at this clinically relevant bone site.

This study has several strengths. To our knowledge, it is the first large randomized clinical trial with a long (2-year) duration that was double-blinded to vitamin D status, evaluating the effectiveness of vitamin D and exercise training in preventing falls and related injuries in older women. Second, withdrawal from the study was low at only 9.5%. Third, pill compliance was excellent, and participation in exercise training was good. Fourth, falls were assessed monthly using fall diaries, and all reported falls were scrutinized by the investigators. Fifth, physical functioning and bone traits were comprehensively assessed. Furthermore, when planning our trial, there was no consensus on the definition of injurious falls. In 2012, Schwenk et al[30] proposed a classification, and our definition conforms with this recommendation.

There were also limitations to our study. Because of the fortification of fluid milk products in Finland, the baseline 25(OH)D levels were likely too high to reveal all potential beneficial effects of the vitamin. It is possible that vitamin D has greater effects on fall risk among women with vitamin D depletion.[9,10,31] On the other hand, all participants had fallen previously and thus were at increased risk of falling, and vitamin D supplementation is now recommended as a means to reduce the risk of falls irrespective of baseline vitamin D levels. Although the exercise program was planned to be suitable and safe for women with musculoskeletal problems, it was challenging to reach and recruit the frailest women. In other words, our participants were in good health and physical condition. Therefore, our results cannot be generalized to frail and institutionalized women or to men.

Conclusions

Given the fact that fall risk is multifactorial, exercise may be the most effective and feasible strategy for preventing injurious falls in community-dwelling older adults replete with vitamin D. Herein, vitamin D increased bone density slightly, and exercise improved physical functioning. While neither treatment reduced the rate of falling, injurious falls more than halved among exercisers with or without vitamin D. Our participants were vitamin D replete, with sufficient calcium intake. Future research is needed to elaborate the role of vitamin D to enhance physical functioning in elderly women.

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