Calcium, vitamin D, or combined supplementation to prevent fractures and falls: systematic review and meta-analysis

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ABSTRACT

OBJECTIVE

To assess the effect of calcium, vitamin D, or combined supplementation on fractures and falls in adults.

DESIGN

Systematic review and meta-analysis.

DATA SOURCES

Trials included in systematic reviews from 2014, three databases (Medline, Embase, CENTRAL) to 19 February 2025, clinical trial registries, abstracts from scientific meetings, and references from included studies.

ELIGIBILITY CRITERIA

Randomised controlled trials comparing calcium, vitamin D, or combined supplementation with placebo or no treatment in adults (≥18 years) not receiving drug treatment for osteoporosis.

DATA EXTRACTION AND SYNTHESIS

The primary outcome was the risk of any fracture. Secondary outcomes included the risk of hip fracture, non-vertebral fracture, vertebral fracture, and falling, as well as the total number of falls. Pairs of reviewers independently screened trials, extracted data, and assessed risk of bias using the second version of Cochrane's risk of bias tool. Findings were synthesised using random effects meta-analyses and appraised using Grading of Recommendations Assessment, Development and Evaluation, with application of thresholds for absolute effects considered important.

RESULTS

This review included 69 trials involving 153 902 participants. Participants in most of the trials were community dwelling (87%) and not at high risk of fractures or falls (73%). For the primary outcome of any fracture, little to no effect was found from use of calcium supplements (11 trials, 9067 participants; risk ratio 0.91, 95% confidence interval 0.81 to 1.01; moderate certainty), vitamin D supplements (36 trials, 92 045 participants; 1.00, 0.95 to 1.06; high certainty), or combined supplementation (15 trials, 51 126 participants; 0.91, 0.84 to 0.99; high certainty). Calcium, vitamin D, or combined supplementation appeared to have little to no effect on other fracture and fall outcomes, based largely on moderate to high certainty of evidence. The findings remained robust after an extensive exploration of heterogeneity across multiple subgroup analyses. Evidence for high risk patients or those requiring residential care was limited for many outcomes for calcium monotherapy and for combined supplementation.

CONCLUSION

Based on absolute risk reductions and thresholds considered clinically meaningful, this review found little to no benefits from use of calcium, vitamin D, or combined supplementation on the prevention of fractures and falls.

SYSTEMATIC REVIEW REGISTRATION

PROSPERO CRD42023483915.

WHAT IS ALREADY KNOWN ON THIS TOPIC

Previous systematic reviews have found no reduction in fractures with calcium or vitamin D monotherapy and inconsistent results with their combined use, and the effect of vitamin D on falls is inconsistent across systematic reviews

Despite these results, many clinicians, guidelines, and regulatory agencies recommend vitamin D supplementation (with or without calcium) for musculoskeletal health

Prescriptions for calcium and vitamin D have increased substantially since the early 2000s

WHAT THIS STUDY ADDS

In this systematic review and meta-analysis of evidence from randomised controlled trials, calcium, vitamin D, or combined supplementation offers little to no benefit on fracture and fall prevention

These findings remained robust after an extensive exploration of heterogeneity across multiple subgroup analyses

The results do not support routine supplementation with calcium or vitamin D, or combined supplementation to prevent fractures and falls

Introduction

Almost a third of older adults (≥65 years) experience at least one fall annually.[1] Falls are the primary cause of both fatal and non-fatal injuries in this population, resulting in increased healthcare utilisation and substantial economic costs.[1 2] As much as 85% of older adults have a fear of falling because of a fall, contributing to reduced daily functioning and increased risk of subsequent falls.[3 4] Furthermore, half of women and one fifth of men will sustain a low trauma fracture during their lifetime, often due to a fall.[5 6] Among older adults, fractures are strongly associated with poor outcomes such as pain, functional impairment, diminished quality of life, increased healthcare utilisation, need for residential care, and economic costs.[6-8] Therefore, preventing falls and fractures has become a global public health priority.[6-10]

Calcium and vitamin D play major roles in regulating bone homoeostasis and muscle cell differentiation, metabolism, and function.[7 11] In observational studies, low dietary calcium intake and low serum

vitamin D levels have been associated with loss of bone mineral density, reduced muscle function, falls, and fractures.[12-17] Since 1990, several randomised controlled trials have assessed whether calcium, vitamin D, or combined supplementation benefits musculoskeletal health.[9 18] Based on initially promising findings,[19-22] vitamin D supplementation (with or without calcium) has been widely recommended to prevent fractures and falls.[10 23-25] A substantial increase in calcium and vitamin D prescriptions has been reported in many countries, leading to high economic burden.[26-32]

Although recent systematic reviews have reached a consensus that calcium or vitamin D supplementation offer no benefit in the prevention of fractures, uncertainty remains about the effect of vitamin D monotherapy on falls and the benefit of combined calcium and vitamin D supplementation.[33-42] The most comprehensive systematic reviews of calcium and vitamin D for musculoskeletal health were published between 2014 and 2019, but these reviews had important limitations,[35 37 38 40-42] including the absence of meta-analyses on the effect of vitamin D combined with calcium,[35 37] exclusion of adults in residential care homes,[38 40] absence of reporting on falls,[37 38 40-42] insufficient subgroup analyses to explore the impact of vitamin D dosing,[38 41 42] and absence of a formal assessment of the certainty of evidence.[35 37 40 42] Since the publication of these reviews, several large scale randomised controlled trials[43 44 45 46] (including 54 383 new participants) have been conducted, highlighting the need for an updated systematic review. We therefore performed a systematic review of randomised controlled trials to assess the effect of calcium, vitamin D, or combined supplementation on reducing the number of fractures and falls in adults compared with placebo or no treatment.

Methods

Standardised reporting and registration

We conducted and reported this systematic review and meta-analysis following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 statement (see supplementary table S1).[47 48] The protocol was registered on PROSPERO and has been previously published.[49] Minor modifications were made to the protocol to clarify the statistical analysis plan, and primarily occurred before data synthesis (see supplementary table S2). All post hoc analyses are described in the paper.

Eligibility criteria

We included randomised controlled trials that enrolled adults (≥18 years), compared the administration of calcium, vitamin D, or combined supplementation versus placebo or no treatment, and reported data on at least one prespecified outcome. The primary outcome was the risk of any fracture. Secondary outcomes included the risk of hip fracture, non-vertebral fracture, vertebral fracture, and falling, as well as the total number of falls.

We excluded trials that focused on osteoporosis drugs, long term corticosteroid treatment, or active vitamin D analogues. Trials that randomised participants to other interventions (eg, exercise training, dietary instructions, hormonal therapy) were also excluded if the intervention was not administered to both arms. We applied no restrictions on type or dose of calcium and vitamin D, number of participants or events, or length of follow-up.

Data sources and search strategy

A comprehensive literature search was conducted to 19 February 2025, with no restrictions on language or publication status. In collaboration with a research librarian, we developed a two step search strategy (see supplementary table S3). Firstly, we searched Medline and Embase (from 2014) to identify systematic reviews assessing the effect of calcium, vitamin D, or combined supplementation on fractures or falls. Next, we searched Medline, Embase, and CENTRAL (from 2017) to identify new trials not captured by the included systematic reviews. We also consulted ClinicalTrials.gov, International Clinical Trials Registry Platform, abstracts from scientific meetings, and reference lists of all included studies.

Study selection and data extraction

Pairs of reviewers independently screened titles and abstracts, assessed full text of potentially eligible studies, and extracted data from eligible studies using a standardised, pretested form. Disagreements were resolved through consensus. Covidence was used for managing citations and extracting data. We contacted study authors when necessary to clarify eligibility and obtain data.

We recorded data on fractures and falls regardless of level of trauma, using the longest available follow-up on treatment and an intention-to-treat approach. When trials included multiple treatment arms, we combined the arms to form a single treatment group. If unpublished data, not obtained through personal communications, were found in another systematic review, we used that review to complete data extraction.

When data on any fracture were not provided, we used data from the largest available group of participants with a new non-vertebral or osteoporotic fracture. If data on total falls was not reported, we prioritised fall data in the order: injurious falls, falls resulting in a healthcare or medical visit, or falls requiring hospital admission. If necessary, rate ratios of falls were manually calculated using the number of falls in each group and the corresponding patient years of follow-up.

Risk of bias

Pairs of reviewers independently assessed risk of bias of eligible studies using Cochrane's risk of bias (RoB 2.0) tool.[50] Disagreements were resolved through consensus. Each domain was classified as having low risk, raising some concerns, or having high risk of bias. The overall risk of bias was determined based on

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the highest risk domain. We used Robvis software to generate figures.

Statistical analysis

Given the clinical heterogeneity expected from study populations and dosing regimens, we conducted random effects meta-analyses using inverse variance weighting models. The Wald-type or Hartung-Knapp-Sidik-Jonkman method was used to pool effect estimates, according to the estimate of heterogeneity and the number of trials included in each meta-analysis.[47] We reported risk ratios for the risk of fracture or falling, and incidence rate ratios for the total number of falls. Trials with no events in both arms were excluded from the meta-analyses.[47] Heterogeneity between trials was quantified by the τ^2 statistic using the restricted maximum likelihood method. The proportion of variability due to heterogeneity was investigated through visual inspection of the forest plots, and the I^2 statistic. All analyses were performed using Cochrane's Review Manager. For each meta-analysis including 10 or more trials, we assessed publication bias using funnel plots and Begg's and Egger's tests with the metafor package in R (version 4.5.0). Asymmetry on the funnel plot or a P<0.05 on one of these tests suggested potential bias.

Subgroup analysis

The subgroup analysis plan was determined based on previous systematic reviews and guidelines and discussions among authors.[33-38 40-42 51-53] The primary subgroup analysis compared trials involving populations at high risk versus those not at high risk. High risk populations were defined as those with a mean age of 80 years or older, requiring residential care, with a fracture or fall history, with a diagnosis of osteoporosis, or with a mean baseline vitamin D deficiency (<25 nmol/L). For every meta-analysis including 10 or more trials, we conducted additional subgroup analyses to explore potential heterogeneity—namely, population characteristics (≥65 years *v* younger, ≥80 years *v* younger, women only *v* men or both sexes, requiring residential care *v* community dwelling, previous *v* no previous fracture, previous *v* no previous fall, with *v* without osteoporosis), mean baseline vitamin D level (<25 nmol/L *v* higher, <50 nmol/L *v* higher) and mean dietary calcium intake (<800 mg *v* higher), vitamin D characteristics (vitamin D_2 *v* D_3, daily to monthly administration *v* intermittent or high doses, <1000 *v* 1000-2000 *v* >2000 units daily, excluding intermittent or high doses), and trial characteristics (≥1000 *v* <1000 participants, ≤1 *v* >1 year of follow-up).

Sensitivity analysis

In sensitivity analyses, we assessed the robustness of our findings by performing fixed effects meta-analyses, excluding trials at high risk of bias, using the leave-one-out method, excluding trials with less than 1000 patient years of follow-up, and excluding trials that allowed non-trial supplementation of calcium or vitamin D. We also performed post hoc sensitivity analyses excluding studies in which osteoporotic or non-vertebral fractures were counted as total fractures, or where a specific subtype of falls (eg, injurious) was used as the falls outcome.

Meta-regression

We conducted post hoc meta-regression analyses using mixed effects models to explore whether baseline and achieved vitamin D levels, treated as continuous covariates, modified treatment effects. These analyses were undertaken to further investigate findings from subgroup analyses and to provide a more nuanced understanding of the clinical relevance of vitamin D levels. We performed meta-regression analyses for each meta-analysis on vitamin D that included 10 or more trials reporting baseline or achieved vitamin D levels. All analyses were conducted using the metafor package in R (version 4.5.0).

GRADE assessment

We used the GRADE (Grading of Recommendations Assessment, Development and Evaluation) approach to rate the certainty of evidence for all findings as high, moderate, low, or very low.[54 55] This approach systematically evaluates risk of bias, indirectness, heterogeneity, imprecision, and publication bias to reflect the certainty that an important effect is truly present. Two authors independently conducted GRADE assessments, with disagreements resolved through consensus. The final assessment was presented to all authors for discussion and approval during a dedicated session. We synthesised results in a modified summary of findings table with standardised plain language summaries.[55]

Imprecision was assessed using a minimally contextualised approach.[56] The minimal clinically important differences were a priori defined as 0.7% absolute reduction for hip fractures, 2% for any fractures, non-vertebral fractures, and vertebral fractures, 3% for risk of falling, and five falls per 100 person years. With no established minimal clinically important differences for fractures and falls, we determined thresholds by author consensus, informed by an unstructured review of literature on clinician and patient preferences on fractures and falls. These thresholds helped assess whether treatment effects were clinically meaningful and aided interpretation of confidence interval (CIs).

Patient and public involvement

No patients or members of the public were involved in the design, conduct, or reporting of this review. Limited funding and time constraints precluded their formal involvement. We acknowledge, however, that this systematic review addresses priorities voiced by older adults during clinical consultations or hospital rounds—specifically the prevention of fractures and falls.

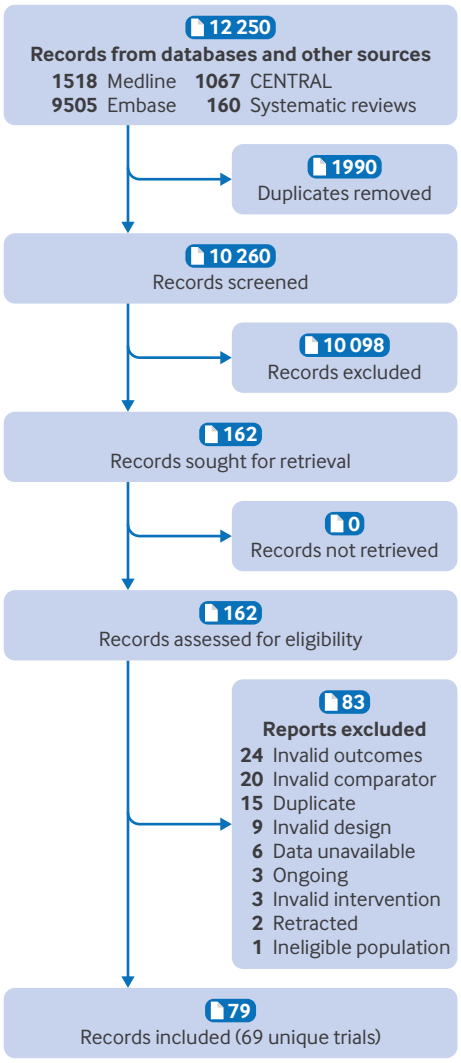

Fig 1 | PRISMA flow diagram of study selection process

Results

Description of included trials

Of 10 260 unique citations, we included 79 reports and 69 trials involving 153 902 participants (fig 1 and supplementary figure S1).[19 20 43-46 57-129] Of the 69 trials, 67 were identified through our search of existing systematic reviews, while the remaining two were retrieved through our database searches. Two trials (including 123 participants) were excluded from the meta-analysis, as they reported no events in both arms.[70 129] We obtained additional data on fractures or falls directly from trial authors for one trial and previous systematic reviews for 13 trials (see supplementary table S4).[20 43 59 67 69 76 77 79 81 86 95 99 103 115]

Table 1 summarises the characteristics of the included trials (see supplementary table S5 for the main characteristics). Most trials (87%, 60/69) were placebo controlled, and 20 trials (29%, 20/69) included co-interventions given to both groups. Of the 69 trials, 23% (16/69) studied calcium monotherapy, 67% (46/69) studied vitamin D monotherapy, and 25% (17/69) studied calcium and vitamin D combined. Vitamin D was mostly administered daily to monthly (71%, 41/58) but occasionally was given in intermittent or high single doses (29%, 17/58). The median follow-up duration across trials was 2.0 years (interquartile range (IQR) 1.0-3.2 years), during which participants received the study interventions. Of the 69 trials, 59% (41/69) reported a mean follow-up of more than one year. Most trials were conducted in Europe (43%, 30/69), North America (23%, 16/69), and Australia or New Zealand, or both (16%, 11/69).

Most trials included community dwelling older adults not at high risk of fractures and falls. The median age across trials was 71.2 (IQR 63.8-76.9) years, with 58 trials (84%) reporting a mean age of at least 65 years. Of the 69 trials, only 28% (19/69) studied high risk populations, 87% (60/69) included only community dwelling adults, and 38% (26/69) recruited only women. A minority of trials included only participants with previous fractures (6%, 4/69), previous falls (4%, 3/69), or osteoporosis diagnosis (6%, 4/69). Most trials (71%, 49/69) reported baseline vitamin D levels. Mean baseline vitamin D levels <50 nmol/L and <25 nmol/L were reported in 32% (22/69) and 3% (2/69) of trials, respectively.

Risk of bias

Of the 69 trials, most were assessed as having high risk of bias (34/59 trials for fracture assessment and 23/48 trials for fall assessment) or raising some concerns (12/59 trials for fracture assessment and 11/48 for fall assessment) (see supplementary figure S2). Supplementary table S6 presents the detailed risk of bias assessment for individual studies.

Most trials (70%, 48/69) reported only non-industry funding, but with drugs supplied by industry in many cases (54%, 26/48). Only 26% (18/69) of trials reported industry funding. Additionally, 40 (58%) trials had unclear or potential conflicts of interests. Supplementary table S7 provides full details on funding sources and conflicts of interest statements.

GRADE assessment, and publication bias

The GRADE assessment is synthesised in one summary of findings table (table 2) and three additional tables (see supplementary tables S8-S10). Overall, the certainty of evidence was moderate to high for 88% (16/18) of findings.

Visual inspection of funnel plots, along with Begg's and Egger's tests, did not indicate important publication bias (see supplementary figures S3-S5).

Effects of the interventions

Calcium monotherapy

Fifteen trials (9435 participants) studied the effect of calcium supplementation over a mean follow-up of 2.8 years (fig 2 and supplementary figure S6).

Calcium supplementation likely has little to no effect on the risk of any fracture (11 trials, 9067 participants; risk ratio 0.91, 95% CI 0.81 to 1.01; moderate certainty of evidence; fig 2). Supplementary figure S6 shows the pooled effects for other fracture types and

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Table 1 | Characteristics of the 69 included trials. Values are number (percentage) of trials unless stated otherwise

Characteristics	Estimates
Year of publication:	
≤2000	12 (17)
2001-10	23 (33)
2011-20	25 (36)
2021-25	9 (13)
Country area:	
North America	16 (23)
South America	1 (1)
Europe	30 (43)
Asia	7 (10)
Australia and/or New Zealand	11 (16)
Africa	1 (1)
Multiple continents	3 (4)
Median (IQR) sample size	327 (134-1460)
Median (IQR) trial follow-up (years)	2.0 (1.0-3.2)
Trial follow-up ≤1 year	28 (41)
Supplementation treatment:	
Vitamin D	46 (67)
Calcium	16 (23)
Calcium and vitamin D	17 (25)
Vitamin D administration*:	
Daily to monthly	41/58 (71)
Intermittent or single high dose	17/58 (29)
Vitamin D dose (daily to monthly (units/day)):	
<1000	23/41 (56)
1000-2000	12/41 (29)
>2000	6/41 (15)
Baseline vitamin D_3 level (nmol/L):	
<25	2 (3)
<50	22 (32)
≥50	27 (39)
Missing	20 (30)
Achieved vitamin D_3 level (nmol/L)†:	
<50	5/58 (9)
≥50	32/58 (55)
≥75	19/58 (33)
Missing	21/58 (36)
Baseline dietary calcium intake (mg/day):	
<800	14 (20)
≥800	20 (21)
Missing	35 (51)
High risk population	19 (28)
Median (IQR) age (years)	71.2 (63.8-76.9)
Age group (years):	
≥65	58 (84)
≥80	11 (16)
Sex:	
Women only	26 (38)
Men only, or both sexes	43 (62)
In residential care home	9 (13)
Previous fractures	4 (6)
Previous falls	3 (4)
Osteoporosis diagnosis	4 (6)

When characteristics were not reported in all trials, the number of trials is shown as No/No of trials (%).
IQR=interquartile range.
*Intermittent or single high doses included any administration of vitamin D involving a loading dose or administration at a frequency higher than monthly.
†Only if vitamin D was administered.

falls. The effect of calcium on the risk of hip fracture is very uncertain (6 trials, 6703 participants; 1.63, 0.86 to 3.03; very low certainty). Calcium likely has little to no effect on the risk of non-vertebral fracture (4 trials, 3204 participants; 0.95, 0.79 to 1.14; moderate certainty), risk of vertebral fracture (10 trials, 6576 participants; 0.82, 0.65 to 1.04; moderate certainty), risk of falling (2 trials, 2966 participants; 0.91, 0.78 to 1.06; moderate certainty), and total number of falls (2 trials, 1794 participants; incidence rate ratio 1.02, 95% CI 0.96 to 1.09; moderate certainty).

We did not identify any credible subgroup effects (see supplementary table S11). In the primary subgroup analyses, we did not find any difference in the treatment effects of calcium in high risk compared with not at high risk populations. Results remained robust after conducting the sensitivity analyses (see supplementary table S12).

Vitamin D monotherapy

Forty six trials (96 296 participants) studied the effect of vitamin D supplementation over a mean follow-up of 2.0 years (fig 3 and supplementary figure S7)

Vitamin D supplementation has little to no effect on the risk of any fracture (36 trials, 92 415 participants; risk ratio 1.00, 95% CI 0.95 to 1.06; high certainty of evidence). Supplementary figure S7 shows the pooled effects for other fracture types and falls. Vitamin D has little to no effect on the risk of hip fracture (15 trials; 72 344 participants; 1.13, 1.00 to 1.27; high certainty), risk of non-vertebral fracture (20 trials, 77 329 participants; 1.01, 0.95 to 1.06; high certainty), vertebral fracture (7 trials, 11 803 participants; 1.04, 0.66 to 1.65; high certainty), risk of falling (32 trials, 65 234 participants; 1.01, 0.98 to 1.04; high certainty), and total number of falls (12 trials, 68 022 participants; incidence rate ratio 1.00, 95% CI 0.95 to 1.06; high certainty).

We did not identify any credible subgroup effects (see supplementary table S13). In the primary subgroup analyses, we did not find any difference in the treatment effects of vitamin D supplementation in high risk compared with not at high risk populations. The post hoc meta-regression models showed no significant association between vitamin D levels and treatment effects (see supplementary figure S8). Results remained robust after conducting the sensitivity analyses (see supplementary table S14).

Calcium and vitamin D combined

Sixteen trials (51 172 participants) studied the effect of combined calcium and vitamin D supplementation over a mean follow-up of 2.3 years (fig 4 and supplementary figure S9)

Combined supplementation has little to no effect on the risk of any fracture (15 trials, 51 126 participants; risk ratio 0.91, 95% CI 0.84 to 0.99; high certainty of evidence). Supplementary figure S9 shows the pooled effects for other fracture types and falls. Combined supplementation also has little to no effect on the risk of hip fracture (9 trials, 49 909 participants; 0.84, 0.74 to 0.96; high certainty) and vertebral fracture (4 trials, 42 185 participants; 0.90, 0.74 to 1.09; high certainty). Combined supplementation likely has little to no effect on the risk of non-vertebral fracture (7 trials, 10 324 participants; 0.87, 0.78 to 0.96; moderate certainty) and risk of falling (10 trials, 11 068 participants;

Table 2 | Summary of findings. Values are percentages unless stated otherwise

Outcomes	Anticipated absolute effect		Absolute risk difference (95% CI)	Relative effect (95% CI)	No of patients (No of trials)	Certainty of evidence (GRADE)	Summary
	Control*	Treatment (95% CI)†					
Calcium versus placebo or no treatment							
Risk of any fracture	10.9	9.9 (8.8 to 11.0)	−1.0 (−2.1 to 0.1)	RR 0.91 (0.81 to 1.01)	9067 (11)	Moderate‡	Likely little to no effect
Risk of hip fracture	1.6	2.6 (1.4 to 4.8)	1.0 (−0.2 to 3.2)	RR 1.63 (0.86 to 3.03)	6703 (6)	Very low§	Very uncertain effect
Risk of non-vertebral fracture	12.5	11.9 (9.9 to 14.3)	−0.6 (−2.6 to 1.8)	RR 0.95 (0.79 to 1.14)	3204 (4)	Moderate¶	Likely little to no effect
Risk of vertebral fracture	4.2	3.4 (2.7 to 4.4)	−1.0 (−1.5 to 0.2)	RR 0.82 (0.65 to 1.04)	6576 (10)	Moderate‡	Likely little to no effect
Risk of falling	17.2	15.7 (13.4 to 18.2)	−1.5 (−3.8 to 1.0)	RR 0.91 (0.78 to 1.06)	2966 (2)	Moderate¶	Likely little to no effect
Total No of falls	59 per 100 patient years	60 per 100 (57 to 64)	1.0 (−2.0 to 3.0)	IRR 1.02 (0.96 to 1.09)	1794 (2)	Moderate‡	Likely little to no effect
Vitamin D versus placebo or no treatment							
Risk of any fracture	6.5	6.5 (6.2 to 6.9)	0.0 (−0.3 to 0.4)	RR 1.00 (0.95 to 1.06)	92 415 (36)	High	Little to no effect
Risk of hip fracture	1.3	1.4 (1.3 to 1.8)	0.1 (0 to 0.5)	RR 1.13 (1.00 to 1.27)	74 344 (15)	High	Little to no effect
Risk of non-vertebral fracture	6.4	6.4 (6.1 to 6.8)	0.5 (−0.3 to 0.4)	RR 1.01 (0.95 to 1.06)	77 329 (20)	High	Little to no effect
Risk of vertebral fracture	1.4	1.4 (0.9 to 2.3)	0.0 (−0.5 to 0.9)	RR 1.04 (0.66 to 1.65)	11 803 (7)	High	Little to no effect
Risk of falling	25.3	25.3 (24.8 to 26.3)	0.0 (−0.5 to 1.0)	RR 1.01 (0.98 to 1.04)	65 234 (32)	High	Little to no effect
Total No of falls	73 per 100 patient years	73 per 100 (69 to 77)	0.0 (−4.0 to 4.0)	IRR 1.00 (0.95 to 1.06)	68 022 (12)	High	Little to no effect
Vitamin D combined with calcium versus placebo or no treatment							
Risk of any fracture	11.3	10.3 (9.5 to 11.2)	−1.0 (−1.8 to −0.1)	RR 0.91 (0.84 to 0.99)	51 126 (15)	High	Little to no effect
Risk of hip fracture	1.8	1.5 (1.3 to 1.7)	−0.3 (−0.5 to −0.1)	RR 0.84 (0.74 to 0.96)	49 909 (9)	High	Little to no effect
Risk of non-vertebral fracture	12.4	10.8 (9.7 to 11.9)	−1.6 (−2.7 to −0.5)	RR 0.87 (0.78 to 0.96)	10 324 (7)	Moderate¶	Likely little to no effect
Risk of vertebral fracture	1.0	0.9 (0.7 to 1.1)	−0.1 (−0.3 to 0.1)	RR 0.90 (0.74 to 1.09)	42 185 (4)	High	Little to no effect
Risk of falling	33.7	31.0 (28.3 to 33.7)	−2.7 (−5.4 to 0.0)	RR 0.92 (0.84 to 1.00)	11 068 (10)	Moderate¶	Likely little to no effect
Total No of falls	40 per 100 patient years	38 per 100 (35 to 41)	−2.0 (−5.0 to 1.0)	IRR 0.95 (0.88 to 1.03)	7532 (4)	Low**	May have little to no effect

CI=confidence interval; GRADE=Grading of Recommendations Assessment, Development and Evaluation; IRR=incidence rate ratio; RR=risk ratio.
*The risk in the control group was estimated using the sample size weighted mean of the control group event rates, calculated by dividing the total number of control group events by the total number of participants in the control arms across all studies in each meta-analysis.
†The risk in the intervention group (and its 95% CI) is based on the assumed risk in the comparison group and the relative effect of the intervention (and its 95% CI).
‡Rated down for risk of bias.
§Rated down for risk of bias, imprecision, and inconsistency.
¶Rated down for imprecision.
**Rated down for risk of bias and imprecision.

0.92, 0.84 to 1.00; moderate certainty) and may have little to no effect on the total number of falls (4 trials, 7532 participants; incidence rate ratio 0.95, 95% CI 0.88 to 1.03; low certainty). Although three meta-analyses showed statistically significant differences, the absolute differences did not reach thresholds considered clinically meaningful; therefore, combined supplementation was judged to provide little to no benefit.

We did not identify any credible subgroup effects (see supplementary table S15). In the primary subgroup analyses, we did not find any difference in the treatment effects of vitamin D combined with calcium in high risk populations compared with those not at high risk. Sensitivity analyses indicated that one study had a disproportionate influence on the overall findings (see supplementary table S16).[19 60] Using a leave-one-out approach, exclusion of this trial slightly attenuated the treatment effect and resulted in a loss of statistical significance for three outcomes. The relative risk for any fracture changed from 0.91 (95% CI 0.84 to 0.99) to 0.96 (0.91 to 1.01), for hip fracture from 0.84 (0.74 to 0.96) to 0.88 (0.75 to 1.05), and for non-vertebral fracture from 0.87 (0.78 to 0.96) to 0.90 (0.78 to 1.05).

Post hoc sensitivity analyses

Results remained robust after conducting the post hoc sensitivity analyses (see supplementary table S17).

Discussion

This systematic review of 69 trials involving 153 902 participants found that calcium, vitamin D, or combined supplementation has little to no effect on fracture and fall prevention, based largely on moderate to high certainty of evidence. Calcium and vitamin D monotherapy did not significantly reduce any outcome, either statistically or clinically. We unexpectedly observed a trend towards a possible increase in hip fractures with calcium monotherapy, but this finding was imprecise and uncertain and biologically implausible.

Three meta-analyses evaluating combined calcium and vitamin D supplementation reported statistically significant treatment effects. The absolute benefits for fracture prevention were, however, lower than the minimal clinically important differences established: 1% fewer fractures at any site (number needed to treat of 100), 0.3% fewer hip fractures (number needed to treat of 333), and 1.6% fewer non-vertebral fractures (number needed to treat of 63). Sensitivity analyses

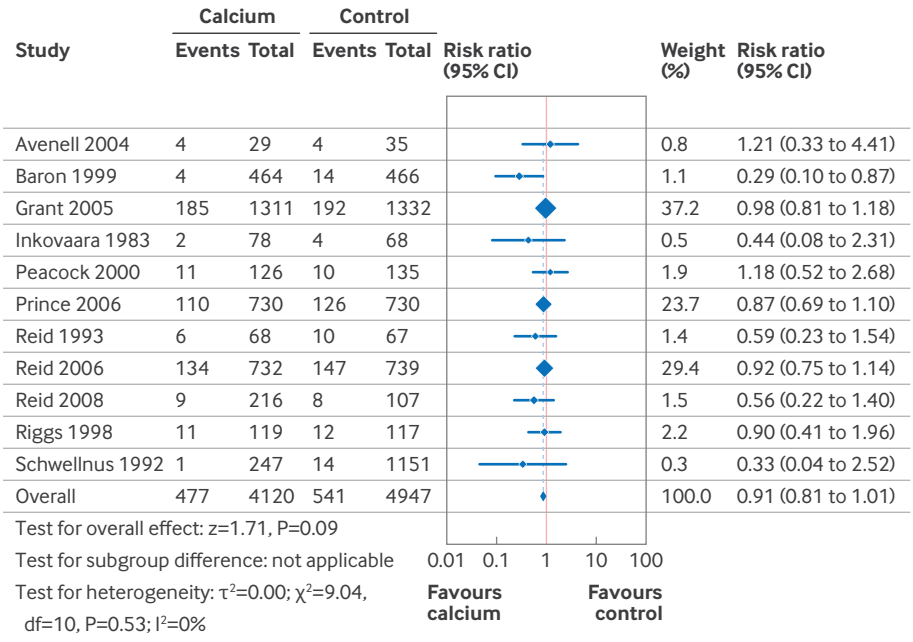

Fig 2 | Pooled effect of calcium supplementation versus placebo or no treatment for risk of any fracture (results for other fracture types and falls are shown in supplementary figure S6). CI=confidence interval; df=degrees of freedom

indicated that these absolute risk reductions were largely explained by one trial conducted in a very high risk population, suggesting that the observed differences would likely be even smaller in the general population.[19 60]

Across the numerous subgroup analyses, we found no consistent evidence of different treatment effects. Evidence for those at high risk or requiring residential care, however, was limited for many outcomes for calcium monotherapy and combined supplementation. Although our analyses included high risk populations, the absolute effects used for our conclusions may somewhat underestimate benefits for such populations, particularly for combined supplementation, and this should be considered when applying the findings to these populations.

Strengths and weaknesses of this systematic review

Strengths of this systematic review include the broad eligibility criteria, a comprehensive search, and pairs of reviewers independently screening studies, extracting data, and assessing risk of bias (ROB 2) and certainty of the evidence (GRADE). Incorporation of recent large scale trials on vitamin D increased statistical power and precision of treatment effects.[43-46] We also explored the effect of key clinical variables through multiple subgroup analyses, including comparisons of trials that enrolled high risk populations versus those not at high risk.

A key limitation of our review is that several of the subgroup analyses included only a small number of trials and participants, and therefore these findings should be interpreted with caution. In addition, we did not perform within trial subgroup analyses, which are considered the most rigorous approach for examining differences across population characteristics. Our interpretation of minimally important differences also has important limitations. To rate the imprecision of absolute effects, we adopted a minimally contextualised approach based on GRADE methodology.[56] We did not, however, involve patient partners in establishing minimally important differences, nor did we identify any clear thresholds to judge the clinical significance of the findings. Accordingly, by consensus, we defined arbitrary absolute effect thresholds for what constitutes important effects, recognising that different teams or clinicians may have alternative definitions of what is clinically meaningful. Finally, another important limitation is the non-generalisability of our findings to people using osteoporosis drugs. Nearly all randomised controlled trials of osteoporosis drugs provide calcium or vitamin D, or both, as background treatment, which is a major reason current clinical guidelines recommend these supplements as co-interventions for such patients.[23 130]

Some limitations of our systematic review reflect inherent limitations of the included trials. Many trials prescribed low doses of vitamin D and enrolled participants not at high risk of fractures or falls, often with normal baseline vitamin D levels. The short duration and small sample sizes of many trials may also have limited the possibility to detect clinically meaningful differences. Nonetheless, treatment effects remained consistent across subgroup analyses, which helps reduce concerns about these important limitations. Importantly, we could not exclude that our findings may be partly explained by personal intake of calcium and vitamin D supplements in control groups, potentially biasing results towards the null. Almost all studies either allowed participants to take non-trial

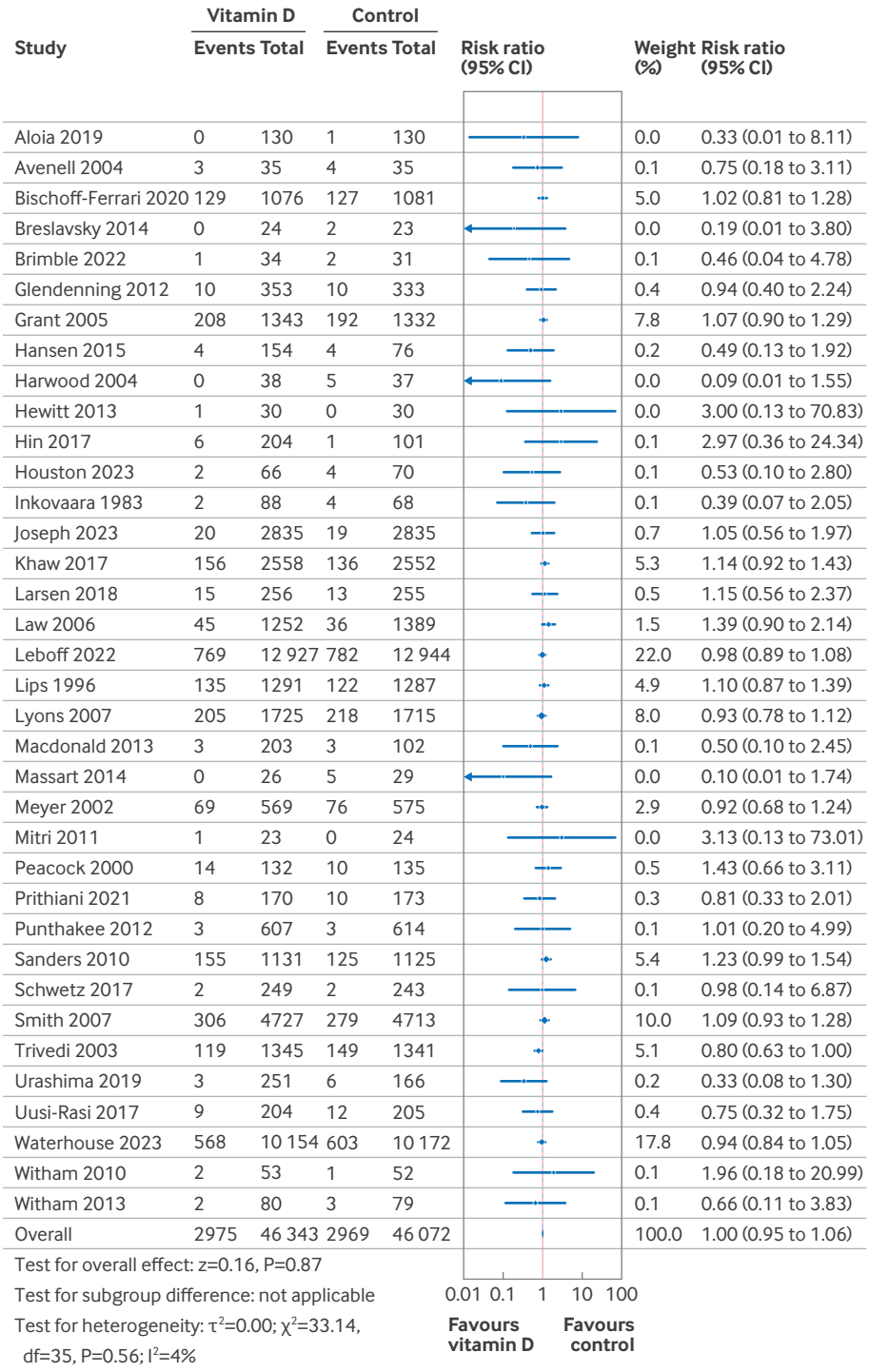

Fig 3 | Pooled effect of vitamin D supplementation versus placebo or no treatment for risk of any fracture (results for other fracture types and falls are shown in supplementary figure S7). CI=confidence interval; df=degrees of freedom

supplements or did not clearly report instructions for avoiding non-trial supplementation.

Results in context

The first major trial investigating vitamin D (with calcium), published in the early 1990s, reported a 17% relative reduction in non-vertebral fractures (absolute reduction of 3.2%) and a 23% relative reduction in hip fractures (absolute reduction of 2.5%) over three years.[19 60] However, this trial enrolled old women (mean age of 84 years) requiring residential care with high risk of hip fracture (11% over three years), low baseline vitamin D levels (mean 20 nmol/L using modern assays), and low dietary calcium intake (mean 513 mg/day), many of whom may have had unrecognised osteomalacia.[37 131] As such, these

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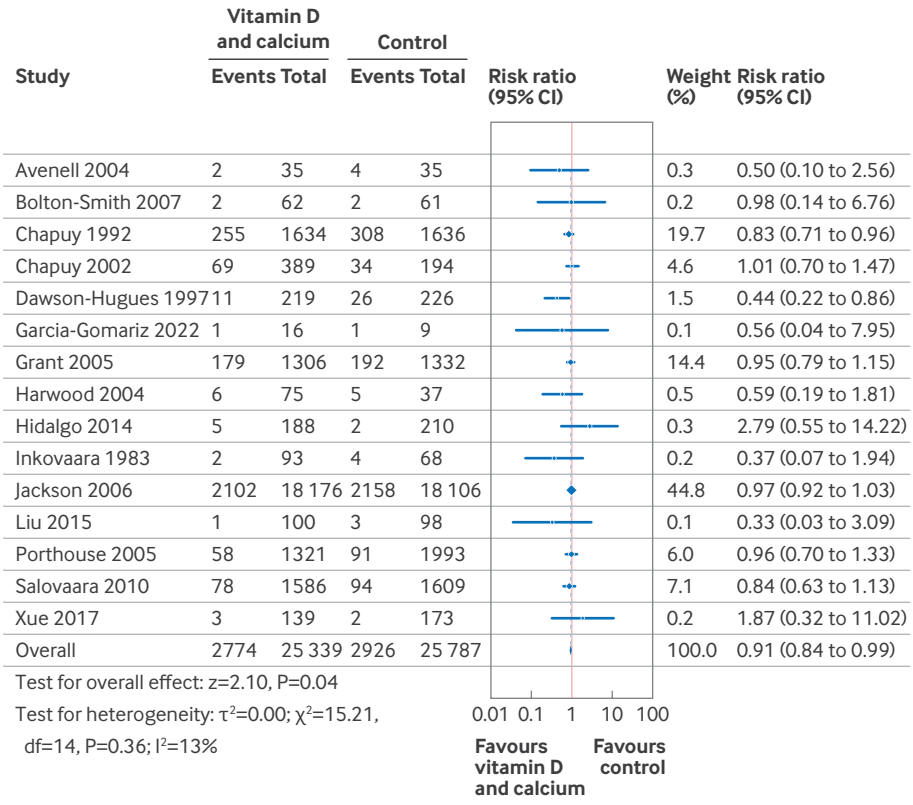

Fig 4 | Pooled effect of combined calcium and vitamin D supplementation versus placebo or no treatment for risk of any fracture (results for other fracture types and falls are shown in supplementary figure S9). CI=confidence interval; df=degrees of freedom

findings, obtained in a high risk population, may not be generalisable to other populations. Nevertheless, this trial generated interest for the musculoskeletal benefits of calcium and vitamin D, although its findings were not replicated in subsequent trials.

In line with these findings, several systematic reviews published in the early 2000s suggested that vitamin D, with or without calcium, might reduce the risk of fractures and falling.[21 22 132-135] Conclusions, however, often relied on a small number of trials, specific dosing regimens or subgroup analyses, or treatment effects with clinically uncertain absolute risk reductions. Early meta-analyses might also have been heavily influenced by two trials with concerns about publication integrity, one of which has since been retracted.[136] Inconsistencies in how trial data were extracted and analysed may have further contributed to positive findings in some meta-analyses.[137]

Most recent systematic reviews provide a contrasting view of the musculoskeletal benefits of vitamin D. An umbrella review evaluating the efficacy of vitamin D for fracture prevention identified 25 systematic reviews and concluded no significant effects with monotherapy and uncertain effects with vitamin D combined with calcium.[33] Recent systematic reviews exploring the effect of vitamin D, with or without calcium, on falls reported conflicting findings.[34-36 39 138-142]

Despite this body of evidence, clinical guidelines continue to promote vitamin D supplementation. A recent systematic review of 34 guidelines published between 2010 and 2020 found that 70% recommended or suggested vitamin D supplements for fracture prevention or general health.[23] Consequently, vitamin D prescriptions have rapidly increased in many countries.[26-32] In the UK alone, prescription costs have increased from £13m ($18m; €15m) in 2001 to £111m in 2021.[32] A recent cost-benefit analysis estimated that providing calcium and vitamin D supplements to all adults aged 50 years and older with osteoporosis in the US and European Union would cost about $2bn annually.[143] The economic burden could be even higher if extended to other countries or populations without osteoporosis.

Some may argue that vitamin D and calcium supplements are generally well tolerated and might provide population level benefits. This rationale does not apply to vitamin D monotherapy, however, as our findings clearly demonstrated no benefit. Furthermore, calcium supplements are often difficult to swallow and poorly tolerated in older adults, commonly causing gastrointestinal adverse effects such as constipation, bloating, abdominal pain, or cramps.[18 144] One study suggested a possible increase in gastrointestinal related hospital admissions associated with calcium supplements, although the absolute risk increase remains unclear.[84] In the Women's Health Initiative trial, calcium and vitamin D supplementation was linked to a higher incidence of kidney calculi, but

with a low absolute risk increase (0.05%).[145] Some data suggest a 10-20% relative increase (0.5-1% absolute increase) in myocardial infarction associated with calcium supplement intake, but meta-analyses reported conflicting results.[146-149]

Implications and future research

Apart from exercise and drug treatments for osteoporosis, few interventions with moderate or high certainty evidence have been consistently shown to reduce the risk of fractures.[130 150] Recent Cochrane reviews of fall prevention strategies found limited or uncertain benefits for most single interventions, although exercise and environmental modifications appear promising.[142 151-154]

Future trials may evaluate interventions other than calcium, vitamin D, or combined supplementation to prevent fractures and falls. Potential areas of investigation include dietary strategies, drug review, educational or behavioural approaches, multicomponent interventions, and digital tools for fall prevention.

Conclusion

Our systematic review found that calcium combined with vitamin D was the only intervention associated with a statistically significant reduction in risk of fractures, while no intervention showed a statistically significant reduction in falls. Based on absolute risk reductions and thresholds considered clinically meaningful, this review found little to no benefits with calcium, vitamin D, or combined supplements on fracture and fall prevention. These findings do not support routine supplementation with calcium, vitamin D, or combined supplementation to prevent fractures or falls. However, the results may not be generalisable to individuals with specific bone disorders or to those receiving drug treatment for osteoporosis or using long term corticosteroids. Clinicians, guideline panels, and regulatory agencies should re-evaluate their general recommendations for calcium and vitamin D supplementation in light of current evidence.

Contributors: OM conceived the study. All authors developed the methods. OM and DRW designed the search strategies. OM searched electronic databases for eligible trials. Pairs of reviewers (from all authors) screened the studies, extracted the data, and assessed the risk of bias. OM carried out the statistical analysis. OM and ND performed the GRADE assessment and interpreted the data. OM drafted the manuscript and acts as the review guarantor. All authors critically revised the article for important intellectual content and gave final approval for the article. The corresponding author attests that all listed authors meet authorship criteria and that no others meeting the criteria have been omitted.

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Ethical approval: Not required.

Data sharing: All the data are available on Borealis at https://doi.org/10.5683/SP3/N98FVW. If you experience difficulties accessing the data or require clarification, please contact the corresponding author.

Transparency: The lead author (OM) affirms that the manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned (and, if relevant, registered) have been explained.

Dissemination to participants and related patient and public communities: We plan to disseminate our findings through various channels to the public, patients, and clinicians, including (among others) traditional media, social media, podcasts for healthcare professionals, and clinical and academic conferences.

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1 Bergen G, Stevens MR, Burns ER. Falls and fall injuries among adults aged ≥65 years - United States, 2014. *MMWR Morb Mortal Wkly Rep* 2016;65:993-8. doi:10.15585/mmwr.mm6537a2
2 Burns ER, Stevens JA, Lee R. The direct costs of fatal and non-fatal falls among older adults - United States. *J Safety Res* 2016;58:99-103. doi:10.1016/j.jsr.2016.05.001
3 Scheffer AC, Schuurmans MJ, van Dijk N, van der Hooft T, de Rooij SE. Fear of falling: measurement strategy, prevalence, risk factors and consequences among older persons. *Age Ageing* 2008;37:19-24. doi:10.1093/ageing/afm169
4 Tinetti ME, Williams CS. The effect of falls and fall injuries on functioning in community-dwelling older persons. *J Gerontol A Biol Sci Med Sci* 1998;53:M112-9. doi:10.1093/gerona/53A.2.M112
5 Department of Health and Human Services - Office of the Surgeon General (US). Bone health and osteoporosis: a report of the Surgeon General. 2004 (cited 20 Aug 2025). https://www.ncbi.nlm.nih.gov/books/NBK45513/
6 GBD 2019 Fracture Collaborators. Global, regional, and national burden of bone fractures in 204 countries and territories, 1990-2019: a systematic analysis from the Global Burden of Disease Study 2019. *Lancet Healthy Longev* 2021;2:e580-92. doi:10.1016/S2666-7568(21)00172-0
7 Compston JE, McClung MR, Leslie WD. Osteoporosis. *Lancet* 2019;393:364-76. doi:10.1016/S0140-6736(18)32112-3
8 Public Health Agency of Canada. Osteoporosis and related fractures in Canada: Report from the Canadian Chronic Disease Surveillance System. 2020 (cited 20 Aug 2025). https://www.canada.ca/en/public-health/services/publications/diseases-conditions/osteoporosis-related-fractures-2020.html
9 Public Health England with the National Falls Prevention Coordination Group member organisations. Falls and fracture consensus statement: Supporting commissioning for prevention. 2017 (cited 20 Aug 2025). https://assets.publishing.service.gov.uk/media/5a7f4316ed915d74e6229625/falls_and_fractures_consensus_statement.pdf
10 Montero-Odasso M, van der Velde N, Martin FC, et al, Task Force on Global Guidelines for Falls in Older Adults. World guidelines for falls prevention and management for older adults: a global initiative. *Age Ageing* 2022;51:afac205. doi:10.1093/ageing/afac205
11 Girgis CM, Clifton-Bligh RJ, Hamrick MW, Holick MF, Gunton JE. The roles of vitamin D in skeletal muscle: form, function, and metabolism. *Endocr Rev* 2013;34:33-83. doi:10.1210/er.2012-1012
12 Bristow SM, Bolland MJ, Gamble GD, Leung W, Reid IR. Dietary calcium intake and change in bone mineral density in older adults: a systematic review of longitudinal cohort studies. *Eur J Clin Nutr* 2022;76:196-205. doi:10.1038/s41430-021-00957-8
13 Bischoff-Ferrari HA, Kiel DP, Dawson-Hughes B, et al. Dietary calcium and serum 25-hydroxyvitamin D status in relation to BMD among U.S. adults. *J Bone Miner Res* 2009;24:935-42. doi:10.1359/jbmr.081242

14 Key TJ, Appleby PN, Spencer EA, Roddam AW, Neale RE, Allen NE. Calcium, diet and fracture risk: a prospective study of 1898 incident fractures among 34 696 British women and men. *Public Health Nutr* 2007;10:1314-20. doi:10.1017/S1368980007696402
15 Visser M, Deeg DJH, Lips P, Longitudinal Aging Study Amsterdam. Low vitamin D and high parathyroid hormone levels as determinants of loss of muscle strength and muscle mass (sarcopenia): the Longitudinal Aging Study Amsterdam. *J Clin Endocrinol Metab* 2003;88:5766-72. doi:10.1210/jc.2003-030604
16 Snijder MB, van Schoor NM, Pluijm SMF, van Dam RM, Visser M, Lips P. Vitamin D status in relation to one-year risk of recurrent falling in older men and women. *J Clin Endocrinol Metab* 2006;91:2980-5. doi:10.1210/jc.2006-0510
17 Feng Y, Cheng G, Wang H, Chen B. The associations between serum 25-hydroxyvitamin D level and the risk of total fracture and hip fracture. *Osteoporos Int* 2017;28:1641-52. doi:10.1007/s00198-017-3955-x
18 Reid IR. Calcium supplementation- efficacy and safety. *Curr Osteoporos Rep* 2025;23:8. doi:10.1007/s11914-025-00904-7
19 Chapuy MC, Arlot ME, Duboeuf F, et al. Vitamin D3 and calcium to prevent hip fractures in elderly women. *N Engl J Med* 1992;327:1637-42. doi:10.1056/NEJM199212033272305
20 Chapuy MC, Pamphile R, Paris E, et al. Combined calcium and vitamin D3 supplementation in elderly women: confirmation of reversal of secondary hyperparathyroidism and hip fracture risk: the Decalyos II study. *Osteoporos Int* 2002;13:257-64. doi:10.1007/s001980200023
21 Bischoff-Ferrari HA, Dawson-Hughes B, Willett WC, et al. Effect of Vitamin D on falls: a meta-analysis. *JAMA* 2004;291:1999-2006. doi:10.1001/jama.291.16.1999
22 Bischoff-Ferrari HA, Willett WC, Wong JB, Giovannucci E, Dietrich T, Dawson-Hughes B. Fracture prevention with vitamin D supplementation: a meta-analysis of randomized controlled trials. *JAMA* 2005;293:2257-64. doi:10.1001/jama.293.18.2257
23 Fraile Navarro D, López García-Franco A, Niño de Guzmán E, et al. Vitamin D recommendations in clinical guidelines: A systematic review, quality evaluation and analysis of potential predictors. *Int J Clin Pract* 2021;75:e14805. doi:10.1111/ijcp.14805
24 Institute of Medicine (US) Committee to Review Dietary Reference Intakes for Vitamin D and Calcium. Dietary reference intakes for calcium and vitamin D. 2011 (cited 20 Aug 2025). https://www.ncbi.nlm.nih.gov/books/NBK56070/
25 Health Canada. Dietary reference intakes tables: Reference values for vitamins. Ottawa: Health Canada. 2025 (cited 20 Aug 2025). https://www.canada.ca/en/health-canada/services/food-nutrition/healthy-eating/dietary-reference-intakes/tables/reference-values-vitamins.html
26 Bailey RL, Dodd KW, Goldman JA, et al. Estimation of total usual calcium and vitamin D intakes in the United States. *J Nutr* 2010;140:817-22. doi:10.3945/jn.109.118539
27 Gahche J, Bailey R, Burt V, et al. Dietary supplement use among U.S. adults has increased since NHANES III (1988-1994). *NCHS Data Brief* 2011;61:1-8.
28 Castro-Lionard K, Dargent-Molina P, Fermanian C, Gonthier R, Cassou B. Use of calcium supplements, vitamin D supplements and specific osteoporosis drugs among French women aged 75-85 years: patterns of use and associated factors. *Drugs Aging* 2013;30:1029-38. doi:10.1007/s40266-013-0121-9
29 Cianferotti L, Parri S, Gronchi G, et al. Changing patterns of prescription in vitamin D supplementation in adults: analysis of a regional dataset. *Osteoporos Int* 2015;26:2695-702. doi:10.1007/s00198-015-3187-x
30 Crowe FL, Jolly K, MacArthur C, et al. Trends in the incidence of testing for vitamin D deficiency in primary care in the UK: a retrospective analysis of The Health Improvement Network (THIN), 2005-2015. *BMJ Open* 2019;9:e028355. doi:10.1136/bmjopen-2018-028355
31 Bolland MJ, Avenell A, Grey A. Vitamin D deficiency, supplementation and testing: have we got it right in New Zealand?*N Z Med J* 2021;134:86-95.
32 Bolland MJ, Avenell A, Smith K, Witham MD, Grey A. Vitamin D supplementation and testing in the UK: costly but ineffective?*BMJ* 2021;372:n484. doi:10.1136/bmj.n484
33 Chakhtoura M, Bacha DS, Gharios C, et al. Vitamin D supplementation and fractures in adults: a systematic umbrella review of meta-analyses of controlled trials. *J Clin Endocrinol Metab* 2022;107:882-98. doi:10.1210/clinem/dgab742
34 Thanapluetiwong S, Chewcharat A, Takkavatakarn K, Praditpornsilpa K, Eiam-Ong S, Susantitaphong P. Vitamin D supplement on prevention of fall and fracture: a meta-analysis of randomized controlled trials. *Medicine (Baltimore)* 2020;99:e21506. doi:10.1097/MD.0000000000021506
35 Bolland MJ, Grey A, Avenell A. Effects of vitamin D supplementation on musculoskeletal health: a systematic review, meta-analysis, and trial sequential analysis. *Lancet Diabetes Endocrinol* 2018;6:847-58. doi:10.1016/S2213-8587(18)30265-1
36 Myung SK, Cho H. Effects of intermittent or single high-dose vitamin D supplementation on risk of falls and fractures: a systematic review and meta-analysis. *Osteoporos Int* 2023;34:1355-67. doi:10.1007/s00198-023-06761-3
37 Bolland MJ, Leung W, Tai V, et al. Calcium intake and risk of fracture: systematic review. *BMJ* 2015;351:h4580. doi:10.1136/bmj.h4580
38 Kahwati LC, Weber RP, Pan H, et al. Vitamin D, calcium, or combined supplementation for the primary prevention of fractures in community-dwelling adults: evidence report and systematic review for the US Preventive Services Task Force. *JAMA* 2018;319:1600-12. doi:10.1001/jama.2017.21640
39 Tan L, He R, Zheng X. Effect of vitamin D, calcium, or combined supplementation on fall prevention: a systematic review and updated network meta-analysis. *BMC Geriatr* 2024;24:390. doi:10.1186/s12877-024-05009-x
40 Zhao JG, Zeng XT, Wang J, Liu L. Association between calcium or vitamin D supplementation and fracture incidence in community-dwelling older adults: a systematic review and meta-analysis. *JAMA* 2017;318:2466-82. doi:10.1001/jama.2017.19344
41 Avenell A, Mak JCS, O'Connell D. Vitamin D and vitamin D analogues for preventing fractures in post-menopausal women and older men. *Cochrane Database Syst Rev* 2014;2014:CD000227.
42 Yao P, Bennett D, Mafham M, et al. Vitamin D and calcium for the prevention of fracture: a systematic review and meta-analysis. *JAMA Netw Open* 2019;2:e1917789. doi:10.1001/jamanetworkopen.2019.17789
43 LeBoff MS, Chou SH, Ratliff KA, et al. Supplemental vitamin D and incident fractures in midlife and older adults. *N Engl J Med* 2022;387:299-309. doi:10.1056/NEJMoa2202106
44 Bischoff-Ferrari HA, Vellas B, Rizzoli R, et al, DO-HEALTH Research Group. Effect of vitamin D supplementation, omega-3 fatty acid supplementation, or a strength-training exercise program on clinical outcomes in older adults: the DO-HEALTH randomized clinical trial. *JAMA* 2020;324:1855-68. doi:10.1001/jama.2020.16909
45 Waterhouse M, Ebeling PR, McLeod DSA, et al. The effect of monthly vitamin D supplementation on fractures: a tertiary outcome from the population-based, double-blind, randomised, placebo-controlled D-Health trial. *Lancet Diabetes Endocrinol* 2023;11:324-32. doi:10.1016/S2213-8587(23)00063-3
46 Joseph P, Pais P, Gao P, et al, International Polycap Study (TIPS)-3 Investigators. Vitamin D supplementation and adverse skeletal and non-skeletal outcomes in individuals at increased cardiovascular risk: Results from the International Polycap Study (TIPS)-3 randomized controlled trial. *Nutr Metab Cardiovasc Dis* 2023;33:434-40. doi:10.1016/j.numecd.2022.11.001
47 Higgins JPT, Thomas J, Chandler J, et al, eds. *Cochrane Handbook for Systematic Reviews of Interventions version 6.4 (updated August 2023)*. Cochrane, 2023.
48 Page MJ, McKenzie JE, Bossuyt PM, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. *BMJ* 2021;372:n71. doi:10.1136/bmj.n71
49 Massé O, Mercurio CM, Dupuis S, et al. Vitamin D and/or calcium to prevent fractures and falls: protocol for a systematic review and meta-analysis. *BMJ Open* 2024;14:e085902. doi:10.1136/bmjopen-2024-085902
50 Sterne JAC, Savović J, Page MJ, et al. RoB 2: a revised tool for assessing risk of bias in randomised trials. *BMJ* 2019;366:l4898. doi:10.1136/bmj.l4898
51 Tang O, Juraschek SP, Appel LJ. Design Features of Randomized Clinical Trials of Vitamin D and Falls: A Systematic Review. *Nutrients* 2018;10:964. doi:10.3390/nu10080964
52 Pludowski P, Holick MF, Grant WB, et al. Vitamin D supplementation guidelines. *J Steroid Biochem Mol Biol* 2018;175:125-35. doi:10.1016/j.jsbmb.2017.01.021
53 DIPART (Vitamin D Individual Patient Analysis of Randomized Trials) Group. Patient level pooled analysis of 68 500 patients from seven major vitamin D fracture trials in US and Europe. *BMJ* 2010;340:b5463. doi:10.1136/bmj.b5463
54 Guyatt G, Oxman AD, Akl EA, et al. GRADE guidelines: 1. Introduction-GRADE evidence profiles and summary of findings tables. *J Clin Epidemiol* 2011;64:383-94. doi:10.1016/j.jclinepi.2010.04.026
55 Santesso N, Glenton C, Dahm P, et al, GRADE Working Group. GRADE guidelines 26: informative statements to communicate the findings of systematic reviews of interventions. *J Clin Epidemiol* 2020;119:126-35. doi:10.1016/j.jclinepi.2019.10.014
56 Zeng L, Brignardello-Petersen R, Hultcrantz M, et al. GRADE Guidance 34: update on rating imprecision using a minimally contextualized approach. *J Clin Epidemiol* 2022;150:216-24. doi:10.1016/j.jclinepi.2022.07.014
57 Inkovaara J, Gothoni G, Halttula R, Heikinheimo R, Tokola O. Calcium, vitamin D and anabolic steroid in treatment of aged bones: double-blind placebo-controlled long-term clinical trial. *Age Ageing* 1983;12:124-30. doi:10.1093/ageing/12.2.124

58 Hansson T, Roos B. The effect of fluoride and calcium on spinal bone mineral content: a controlled, prospective (3 years) study. *Calcif Tissue Int* 1987;40:315-7. doi:10.1007/BF02556692
59 Reid IR, Ames RW, Evans MC, Gamble GD, Sharpe SJ. Effect of calcium supplementation on bone loss in postmenopausal women. *N Engl J Med* 1993;328:460-4. doi:10.1056/NEJM199302183280702
60 Chapuy MC, Arlot ME, Delmas PD, Meunier PJ. Effect of calcium and cholecalciferol treatment for three years on hip fractures in elderly women. *BMJ* 1994;308:1081-2. doi:10.1136/bmj.308.6936.1081
61 Schwellnus MP, Jordaan G. Does calcium supplementation prevent bone stress injuries? A clinical trial. *Int J Sport Nutr* 1992;2:165-74. doi:10.1123/ijsn.2.2.165
62 Reid IR, Ames RW, Evans MC, Gamble GD, Sharpe SJ. Long-term effects of calcium supplementation on bone loss and fractures in postmenopausal women: a randomized controlled trial. *Am J Med* 1995;98:331-5. doi:10.1016/S0002-9343(99)80310-6
63 Graafmans WC, Ooms ME, Hofstee HM, Bezemer PD, Bouter LM, Lips P. Falls in the elderly: a prospective study of risk factors and risk profiles. *Am J Epidemiol* 1996;143:1129-36. doi:10.1093/oxfordjournals.aje.a008690
64 Lips P, Graafmans WC, Ooms ME, Bezemer PD, Bouter LM. Vitamin D supplementation and fracture incidence in elderly persons. A randomized, placebo-controlled clinical trial. *Ann Intern Med* 1996;124:400-6. doi:10.7326/0003-4819-124-4-199602150-00003
65 Riggs BL, O'Fallon WM, Muhs J, O'Connor MK, Kumar R, Melton LJ3rd. Long-term effects of calcium supplementation on serum parathyroid hormone level, bone turnover, and bone loss in elderly women. *J Bone Miner Res* 1998;13:168-74. doi:10.1359/jbmr.1998.13.2.168
66 Recker RR, Hinders S, Davies KM, et al. Correcting calcium nutritional deficiency prevents spine fractures in elderly women. *J Bone Miner Res* 1996;11:1961-6. doi:10.1002/jbmr.5650111218
67 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. doi:10.1056/NEJM199709043371003
68 Bischoff-Ferrari HA, Orav EJ, Dawson-Hughes B. Effect of cholecalciferol plus calcium on falling in ambulatory older men and women: a 3-year randomized controlled trial. *Arch Intern Med* 2006;166:424-30. doi:10.1001/archinte.166.4.424
69 Baron JA, Beach M, Mandel JS, et al, Calcium Polyp Prevention Study Group. Calcium supplements for the prevention of colorectal adenomas. *N Engl J Med* 1999;340:101-7. doi:10.1056/NEJM199901143400204
70 Ruml LA, Sakhaee K, Peterson R, Adams-Huet B, Pak CY. The effect of calcium citrate on bone density in the early and mid-postmenopausal period: a randomized placebo-controlled study. *Am J Ther* 1999;6:303-11. doi:10.1097/00045391-199911000-00004
71 Peacock M, Liu G, Carey M, et al. Effect of calcium or 25OH vitamin D3 dietary supplementation on bone loss at the hip in men and women over the age of 60. *J Clin Endocrinol Metab* 2000;85:3011-9.
72 Chapuy MC, Pamphile R, Paris E, et al. Combined calcium and vitamin D3 supplementation in elderly women: confirmation of reversal of secondary hyperparathyroidism and hip fracture risk: the Decalyos II study. *Osteoporos Int* 2002;13:257-64. doi:10.1007/s001980200023
73 Meyer HE, 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. doi:10.1359/jbmr.2002.17.4.709
74 Latham NK, Anderson CS, Lee A, Bennett DA, Moseley A, Cameron ID, Fitness Collaborative Group. A randomized, controlled trial of quadriceps resistance exercise and vitamin D in frail older people: the Frailty Interventions Trial in Elderly Subjects (FITNESS). *J Am Geriatr Soc* 2003;51:291-9. doi:10.1046/j.1532-5415.2003.51101.x
75 Trivedi DP, Doll R, Khaw KT. Effect of four monthly oral vitamin D3 (cholecalciferol) supplementation on fractures and mortality in men and women living in the community: randomised double blind controlled trial. *BMJ* 2003;326:469. doi:10.1136/bmj.326.7387.469
76 Avenell A, Grant AM, McGee M, McPherson G, Campbell MK, McGee MA, RECORD Trial Management Group. The effects of an open design on trial participant recruitment, compliance and retention--a randomized controlled trial comparison with a blinded, placebo-controlled design. *Clin Trials* 2004;1:490-8. doi:10.1191/1740774504cn053oa
77 Dhesi JK, Jackson SHD, Bearne LM, et al. Vitamin D supplementation improves neuromuscular function in older people who fall. *Age Ageing* 2004;33:589-95. doi:10.1093/ageing/afh209
78 Fujita T, Ohue M, Fujii Y, Miyauchi A, Takagi Y. Reappraisal of Katsuragi calcium study, a prospective, double-blind, placebo-controlled study of the effect of active absorbable algal calcium (AAACa) on vertebral deformity and fracture. *J Bone Miner Metab* 2004;22:32-8. doi:10.1007/s00774-003-0445-3
79 Harwood RH, Sahota O, Gaynor K, Masud T, Hosking DJ, Nottingham Neck of Femur (NONOF) Study. A randomised, controlled comparison of different calcium and vitamin D supplementation regimens in elderly women after hip fracture: The Nottingham Neck of Femur (NONOF) Study. *Age Ageing* 2004;33:45-51. doi:10.1093/ageing/afh002
80 Grant AM, Avenell A, Campbell MK, et al, 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. doi:10.1016/S0140-6736(05)63013-9
81 Porthouse J, Cockayne S, King C, et al. Randomised controlled trial of calcium and supplementation with cholecalciferol (vitamin D3) for prevention of fractures in primary care. *BMJ* 2005;330:1003. doi:10.1136/bmj.330.7498.1003
82 Jackson RD, LaCroix AZ, Gass M, et al, Women's Health Initiative Investigators. Calcium plus vitamin D supplementation and the risk of fractures. *N Engl J Med* 2006;354:669-83. doi:10.1056/NEJMoa055218
83 Law M, Withers H, Morris J, Anderson F. Vitamin D supplementation and the prevention of fractures and falls: results of a randomised trial in elderly people in residential accommodation. *Age Ageing* 2006;35:482-6. doi:10.1093/ageing/afj080
84 Prince RL, Devine A, Dhaliwal SS, Dick IM. Effects of calcium supplementation on clinical fracture and bone structure: results of a 5-year, double-blind, placebo-controlled trial in elderly women. *Arch Intern Med* 2006;166:869-75. doi:10.1001/archinte.166.8.869
85 Reid IR, Mason B, Horne A, et al. Randomized controlled trial of calcium in healthy older women. *Am J Med* 2006;119:777-85. doi:10.1016/j.amjmed.2006.02.038
86 Bolton-Smith C, McMurdo MET, Paterson CR, et al. Two-year randomized controlled trial of vitamin K1 (phylloquinone) and vitamin D3 plus calcium on the bone health of older women. *J Bone Miner Res* 2007;22:509-19. doi:10.1359/jbmr.070116
87 Broe KE, Chen TC, Weinberg J, Bischoff-Ferrari HA, Holick MF, Kiel DP. A higher dose of vitamin d reduces the risk of falls in nursing home residents: a randomized, multiple-dose study. *J Am Geriatr Soc* 2007;55:234-9. doi:10.1111/j.1532-5415.2007.01048.x
88 Lyons RA, Johansen A, Brophy S, et al. Preventing fractures among older people living in institutional care: a pragmatic randomised double blind placebo controlled trial of vitamin D supplementation. *Osteoporos Int* 2007;18:811-8. doi:10.1007/s00198-006-0309-5
89 Smith H, Anderson F, Raphael H, Maslin P, Crozier S, Cooper C. Effect of annual intramuscular vitamin D on fracture risk in elderly men and women--a population-based, randomized, double-blind, placebo-controlled trial. *Rheumatology (Oxford)* 2007;46:1852-7. doi:10.1093/rheumatology/kem240
90 Reid IR, Ames R, Mason B, et al. Randomized controlled trial of calcium supplementation in healthy, nonosteoporotic, older men. *Arch Intern Med* 2008;168:2276-82. doi:10.1001/archinte.168.20.2276
91 Bischoff-Ferrari HA, Rees JR, Grau MV, Barry E, Gui J, Baron JA. Effect of calcium supplementation on fracture risk: a double-blind randomized controlled trial. *Am J Clin Nutr* 2008;87:1945-51. doi:10.1093/ajcn/87.6.1945
92 Salovaara K, Tuppurainen M, Kärkkäinen M, et al. Effect of vitamin D(3) and calcium on fracture risk in 65- to 71-year-old women: a population-based 3-year randomized, controlled trial--the OSTPRE-FPS. *J Bone Miner Res* 2010;25:1487-95. doi:10.1002/jbmr.48
93 Kärkkäinen MK, Tuppurainen M, Salovaara K, et al. Does daily vitamin D 800 IU and calcium 1000 mg supplementation decrease the risk of falling in ambulatory women aged 65-71 years? A 3-year randomized population-based trial (OSTPRE-FPS). *Maturitas* 2010;65:359-65. doi:10.1016/j.maturitas.2009.12.018
94 Sanders KM, Stuart AL, Williamson EJ, et al. Annual high-dose oral vitamin D and falls and fractures in older women: a randomized controlled trial. *JAMA* 2010;303:1815-22. doi:10.1001/jama.2010.594
95 Witham MD, Crighton LJ, Gillespie ND, Struthers AD, McMurdo MET. The effects of vitamin D supplementation on physical function and quality of life in older patients with heart failure: a randomized controlled trial. *Circ Heart Fail* 2010;3:195-201. doi:10.1161/CIRCHEARTFAILURE.109.907899
96 Mitri J, Dawson-Hughes B, Hu FB, Pittas AG. Effects of vitamin D and calcium supplementation on pancreatic β cell function, insulin sensitivity, and glycemia in adults at high risk of diabetes: the Calcium and Vitamin D for Diabetes Mellitus (CaDDM) randomized controlled trial. *Am J Clin Nutr* 2011;94:486-94. doi:10.3945/ajcn.111.011684
97 Glendenning P, Zhu K, Inderjeeth C, Howat P, Lewis JR, Prince RL. Effects of three-monthly oral 150,000 IU cholecalciferol supplementation on falls, mobility, and muscle strength in older postmenopausal women: a randomized controlled trial. *J Bone Miner Res* 2012;27:170-6. doi:10.1002/jbmr.524

98 Punthakee Z, Bosch J, Dagenais G, et al, TIDE Trial Investigators. Design, history and results of the Thiazolidinedione Intervention with vitamin D Evaluation (TIDE) randomised controlled trial. *Diabetologia* 2012;55:36-45. doi:10.1007/s00125-011-2357-4
99 Breslavsky A, Frand J, Matas Z, Boaz M, Barnea Z, Shargorodsky M. Effect of high doses of vitamin D on arterial properties, adiponectin, leptin and glucose homeostasis in type 2 diabetic patients. *Clin Nutr* 2013;32:970-5. doi:10.1016/j.clnu.2013.01.020
100 Hewitt NA, O'Connor AA, O'Shaughnessy DV, Elder GJ. Effects of cholecalciferol on functional, biochemical, vascular, and quality of life outcomes in hemodialysis patients. *Clin J Am Soc Nephrol* 2013;8:1143-9. doi:10.2215/CJN.02840312
101 Wood AD, Secombes KR, Thies F, et al. A parallel group double-blind RCT of vitamin D3 assessing physical function: is the biochemical response to treatment affected by overweight and obesity?*Osteoporos Int* 2014;25:305-15. doi:10.1007/s00198-013-2473-8
102 Macdonald HM, Wood AD, Aucott LS, et al. Hip bone loss is attenuated with 1000 IU but not 400 IU daily vitamin D3: a 1-year double-blind RCT in postmenopausal women. *J Bone Miner Res* 2013;28:2202-13. doi:10.1002/jbmr.1959
103 Witham MD, Price RJG, Struthers AD, et al. Cholecalciferol treatment to reduce blood pressure in older patients with isolated systolic hypertension: the VitDISH randomized controlled trial. *JAMA Intern Med* 2013;173:1672-9. doi:10.1001/jamainternmed.2013.9043
104 López-Torres Hidalgo J, Grupo ANVITAD. Efecto del calcio y la vitamina D en la reducción de caídas de las personas mayores: ensayo clínico aleatorizado frente a placebo. *Med Clin (Barc)* 2014;142:95-102. doi:10.1016/j.medcli.2012.11.025
105 Massart A, Debelle FD, Racapé J, et al. Biochemical parameters after cholecalciferol repletion in hemodialysis: results From the VitaDial randomized trial. *Am J Kidney Dis* 2014;64:696-705. doi:10.1053/j.ajkd.2014.04.020
106 Hansen KE, Johnson RE, Chambers KR, et al. Treatment of vitamin D insufficiency in postmenopausal women: a randomized clinical trial. *JAMA Intern Med* 2015;175:1612-21. doi:10.1001/jamainternmed.2015.3874
107 Liu BX, Chen SP, Li YD, et al. The effect of the modified eighth section of eight-section brocade on osteoporosis in postmenopausal women: a prospective randomized trial. *Medicine (Baltimore)* 2015;94:e991. doi:10.1097/MD.0000000000000991
108 Cangussu LM, Nahas-Neto J, Orsatti CL, et al. Effect of isolated vitamin D supplementation on the rate of falls and postural balance in postmenopausal women fallers: a randomized, double-blind, placebo-controlled trial. *Menopause* 2016;23:267-74. doi:10.1097/GME.0000000000000525
109 Imaoka M, Higuchi Y, Todo E, Kitagwa T, Ueda T. Low-frequency exercise and vitamin D supplementation reduce falls among institutionalized frail elderly. *Int J Gerontol* 2016;10:202-6doi:10.1016/j.ijge.2016.02.005.
110 Jin X, Jones G, Cicuttini F, et al. Effect of vitamin D supplementation on tibial cartilage volume and knee pain among patients with symptomatic knee osteoarthritis: a randomized clinical trial. *JAMA* 2016;315:1005-13. doi:10.1001/jama.2016.1961
111 Hin H, Tomson J, Newman C, et al. Optimum dose of vitamin D for disease prevention in older people: BEST-D trial of vitamin D in primary care. *Osteoporos Int* 2017;28:841-51. doi:10.1007/s00198-016-3833-y
112 Khaw KT, Stewart AW, Waayer D, et al. Effect of monthly high-dose vitamin D supplementation on falls and non-vertebral fractures: secondary and post-hoc outcomes from the randomised, double-blind, placebo-controlled ViDA trial. *Lancet Diabetes Endocrinol* 2017;5:438-47. doi:10.1016/S2213-8587(17)30103-1
113 Levis S, Gómez-Marín O. Vitamin D and physical function in sedentary older men. *J Am Geriatr Soc* 2017;65:323-31. doi:10.1111/jgs.14510
114 Schwetz V, Schnedl C, Urbanic-Purkart T, et al. Effect of vitamin D3 on bone turnover markers in critical illness: post hoc analysis from the VITdAL-ICU study. *Osteoporos Int* 2017;28:3347-54. doi:10.1007/s00198-017-4190-1
115 Uusi-Rasi K, Patil R, Karinkanta S, et al. A 2-year follow-up after a 2-year RCT with vitamin D and exercise: effects on falls, injurious falls and physical functioning among older women. *J Gerontol A Biol Sci Med Sci* 2017;72:1239-45. doi:10.1093/gerona/glx044
116 Xue Y, Hu Y, Wang O, et al. Effects of enhanced exercise and combined vitamin D and calcium supplementation on muscle strength and fracture risk in postmenopausal chinese women. *Zhongguo Yi Xue Ke Xue Yuan Xue Bao* 2017;39:345-51.
117 Larsen AU, Grimnes G, Jorde R. The effect of high-dose vitamin D_3 supplementation on bone mineral density in subjects with prediabetes. *Osteoporos Int* 2018;29:171-80. doi:10.1007/s00198-017-4222-x
118 Aloia JF, Rubinova R, Fazzari M, Islam S, Mikhail M, Ragolia L. Vitamin D and falls in older African American women: the PODA randomized clinical trial. *J Am Geriatr Soc* 2019;67:1043-9. doi:10.1111/jgs.15760
119 Shea MK, Fielding RA, Dawson-Hughes B. The effect of vitamin D supplementation on lower-extremity power and function in older adults: a randomized controlled trial. *Am J Clin Nutr* 2019;109:369-79. doi:10.1093/ajcn/nqy290
120 Urashima M, Ohdaira H, Akutsu T, et al. Effect of vitamin D supplementation on relapse-free survival among patients with digestive tract cancers: the AMATERASU randomized clinical trial. *JAMA* 2019;321:1361-9. doi:10.1001/jama.2019.2210
121 Bischoff-Ferrari HA, Freystätter G, Vellas B, et al, DO-HEALTH Research Group. Effects of vitamin D, omega-3 fatty acids, and a simple home strength exercise program on fall prevention: the DO-HEALTH randomized clinical trial. *Am J Clin Nutr* 2022;115:1311-21. doi:10.1093/ajcn/nqac022
122 Prithiani SL, Kumar R, Mirani SH, et al. Effect of monthly 100 000 IU vitamin D supplementation on falls and non-vertebral fractures. *Cureus* 2021;13:e12445.
123 LeBoff MS, Murata EM, Cook NR, et al. VITamin D and omegA-3 triaL (VITAL): effects of vitamin D supplements on risk of falls in the US population. *J Clin Endocrinol Metab* 2020;105:2929-38. doi:10.1210/clinem/dgaa311
124 Brimble KS, Ganame J, Margetts P, et al. Impact of bioelectrical impedance-guided fluid management and vitamin D supplementation on left ventricular mass in patients receiving peritoneal dialysis: a randomized controlled trial. *Am J Kidney Dis* 2022;79:820-31. doi:10.1053/j.ajkd.2021.08.022
125 García-Gomariz C, Igual-Camacho C, Sanchís-Sales E, Hernández-Guillén D, Blasco JM. Effects of three interventions combining impact or walking at intense pace training, with or without calcium and vitamin supplements, to manage postmenopausal women with osteopenia and osteoporosis. *Int J Environ Res Public Health* 2022;19:11215. doi:10.3390/ijerph191811215
126 Houston DK, Marsh AP, Neiberg RH, et al. Vitamin D supplementation and muscle power, strength and physical performance in older adults: a randomized controlled trial. *Am J Clin Nutr* 2023;117:1086-95. doi:10.1016/j.ajcnut.2023.04.021
127 Waterhouse M, Sanguineti E, Baxter C, et al. Vitamin D supplementation and risk of falling: outcomes from the randomized, placebo-controlled D-Health Trial. *J Cachexia Sarcopenia Muscle* 2021;12:1428-39. doi:10.1002/jcsm.12759
128 Bischoff-Ferrari HA, Kistler-Fischbacher M, Gaengler S, et al. Effects of testosterone and vitamin D on fall risk in pre-frail hypogonadal men: a factorial design RCT. *J Nutr Health Aging* 2024;28:100217. doi:10.1016/j.jnha.2024.100217
129 Bowles SD, Jacques R, Hill TR, Eastell R, Walsh JS. Effects of high dose bolus cholecalciferol on free vitamin D metabolites, bone turnover markers and physical function. *Nutrients* 2024;16:2888. doi:10.3390/nu16172888
130 Morin SN, Feldman S, Funnell L, et al, Osteoporosis Canada 2023 Guideline Update Group. Clinical practice guideline for management of osteoporosis and fracture prevention in Canada: 2023 update. *CMAJ* 2023;195:E1333-48. doi:10.1503/cmaj.221647
131 Lips P, Chapuy MC, Dawson-Hughes B, Pols HA, Holick MF. An international comparison of serum 25-hydroxyvitamin D measurements. *Osteoporos Int* 1999;9:394-7. doi:10.1007/s001980050162
132 Bischoff-Ferrari HA, Dawson-Hughes B, Staehelin HB, et al. Fall prevention with supplemental and active forms of vitamin D: a meta-analysis of randomised controlled trials. *BMJ* 2009;339:b3692. doi:10.1136/bmj.b3692
133 Bischoff-Ferrari HA, Willett WC, Wong JB, et al. Prevention of nonvertebral fractures with oral vitamin D and dose dependency: a meta-analysis of randomized controlled trials. *Arch Intern Med* 2009;169:551-61. doi:10.1001/archinternmed.2008.600
134 Kalyani RR, Stein B, Valiyil R, Manno R, Maynard JW, Crews DC. Vitamin D treatment for the prevention of falls in older adults: systematic review and meta-analysis. *J Am Geriatr Soc* 2010;58:1299-310. doi:10.1111/j.1532-5415.2010.02949.x
135 Murad MH, Elamin KB, Abu Elnour NO, et al. Clinical review: The effect of vitamin D on falls: a systematic review and meta-analysis. *J Clin Endocrinol Metab* 2011;96:2997-3006. doi:10.1210/jc.2011-1193
136 Bolland MJ, Avenell A, Grey A. Publication integrity: what is it, why does it matter, how it is safeguarded and how could we do better?*J R Soc N Z* 2024;55:267-86. doi:10.1080/03036758.2024.2325004
137 Bolland MJ, Grey A, Reid IR. Differences in overlapping meta-analyses of vitamin D supplements and falls. *J Clin Endocrinol Metab* 2014;99:4265-72. doi:10.1210/jc.2014-2562
138 Octary T, Gautama MSN, Duong H. Effectiveness of vitamin D supplements in reducing the risk of falls among older adults: a meta-analysis of randomized controlled trials. *Ann Geriatr Med Res* 2023;27:192-203. doi:10.4235/agmr.23.0047
139 Kong SH, Jang HN, Kim JH, Kim SW, Shin CS. Effect of vitamin D supplementation on risk of fractures and falls according to dosage and interval: a meta-analysis. *Endocrinol Metab (Seoul)* 2022;37:344-58. doi:10.3803/EnM.2021.1374

140 Ling Y, Xu F, Xia X, et al. Vitamin D supplementation reduces the risk of fall in the vitamin D deficient elderly: An updated meta-analysis. *Clin Nutr* 2021;40:5531-7. doi:10.1016/j.clnu.2021.09.031
141 Wu H, Pang Q. The effect of vitamin D and calcium supplementation on falls in older adults: A systematic review and meta-analysis. *Orthopade* 2017;46:729-36. doi:10.1007/s00132-017-3446-y
142 Dyer SM, Kwok WS, Suen J, et al. Interventions for preventing falls in older people in care facilities. *Cochrane Database Syst Rev* 2025;8:CD016064.
143 Weaver CM, Bischoff-Ferrari HA, Shanahan CJ. Cost-benefit analysis of calcium and vitamin D supplements. *Arch Osteoporos* 2019;14:50. doi:10.1007/s11657-019-0589-y
144 Punzalan C, Budnitz DS, Chirtel SJ, et al. Swallowing Problems and Dietary Supplements: Data From U.S. Food and Drug Administration Adverse Event Reports, 2006-2015. *Ann Intern Med* 2019;171:771-3. doi:10.7326/M19-0947
145 Wallace RB, Wactawski-Wende J, O'Sullivan MJ, et al. Urinary tract stone occurrence in the Women's Health Initiative (WHI) randomized clinical trial of calcium and vitamin D supplements. *Am J Clin Nutr* 2011;94:270-7. doi:10.3945/ajcn.110.003350
146 Yang C, Shi X, Xia H, et al. The evidence and controversy between dietary calcium intake and calcium supplementation and the risk of cardiovascular disease: a systematic review and meta-analysis of cohort studies and randomized controlled trials. *J Am Coll Nutr* 2020;39:352-70. doi:10.1080/07315724.2019.1649219
147 Bolland MJ, Avenell A, Baron JA, et al. Effect of calcium supplements on risk of myocardial infarction and cardiovascular events: meta-analysis. *BMJ* 2010;341:c3691. doi:10.1136/bmj.c3691
148 Lewis JR, Radavelli-Bagatini S, Rejnmark L, et al. The effects of calcium supplementation on verified coronary heart disease hospitalization and death in postmenopausal women: a collaborative meta-analysis of randomized controlled trials. *J Bone Miner Res* 2015;30:165-75. doi:10.1002/jbmr.2311
149 Mao PJ, Zhang C, Tang L, et al. Effect of calcium or vitamin D supplementation on vascular outcomes: a meta-analysis of randomized controlled trials. *Int J Cardiol* 2013;169:106-11. doi:10.1016/j.ijcard.2013.08.055
150 Ayers C, Kansagara D, Lazur B, Fu R, Kwon A, Harrod C. Effectiveness and safety of treatments to prevent fractures in people with low bone mass or primary osteoporosis: a living systematic review and network meta-analysis for the American College of Physicians. *Ann Intern Med* 2023;176:182-95. doi:10.7326/M22-0684
151 Lewis SR, McGarrigle L, Pritchard MW, et al. Population-based interventions for preventing falls and fall-related injuries in older people. *Cochrane Database Syst Rev* 2024;1:CD013789.
152 Drahota A, Udell JE, Mackenzie H, Pugh MT. Psychological and educational interventions for preventing falls in older people living in the community. *Cochrane Database Syst Rev* 2024;10:CD013480.
153 Clemson L, Stark S, Pighills AC, et al. Environmental interventions for preventing falls in older people living in the community. *Cochrane Database Syst Rev* 2023;3:CD013258.
154 Sherrington C, Fairhall NJ, Wallbank GK, et al. Exercise for preventing falls in older people living in the community. *Cochrane Database Syst Rev* 2019;1:CD012424. doi:10.1002/14651858.CD012424.pub2

Supplementary information: Additional figures and tables