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# Effect of vitamin D supplementation alone or with calcium on adiposity measures: a meta-analysis of randomized controlled trials

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## Abstract

**Objective—**Assess vitamin D supplementation alone or with calcium alters adiposity measures.

**Methods—**Systematic search (1966-March 2014) of MEDLINE, EMBASE, and the Cochrane Central Register of Controlled Trials for randomized clinical trials (RCTs) with >50 participants aged ≥18 years at baseline and at least 12 weeks of treatment. Primary end points were changes in weight, body mass index (BMI), or fat mass (FM).

**Results—**Of 953 trials identified, 26 RCTs (12:Vitamin D alone; 10: Vitamin D plus calcium versus calcium control; 4:Vitamin D plus calcium versus placebo) met the inclusion criteria;

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42,430 participants (median duration: 12 months). Vitamin D supplementation alone versus placebo: no significant change in BMI (weighted mean difference (WMD): −0.06 kg/m2, 95% CI: −0.14,0.03), weight (WMD: −0.05 kg, 95% CI:−0.32,0.23) or FM (WMD: −0.43 kg, 95% CI: −1.69,0.84). Vitamin D plus calcium versus calcium control: no significant reduction in BMI (WMD: 0.02 kg/m2, 95% CI: −0.11, 0.14), weight (WMD: 0.12 kg, 95% CI: −0.24, 0.49), or FM (WMD: 0.12 kg, 95% CI: −0.22, 0.45); no significant heterogeneity.

**Conclusions—**Vitamin D showed no effect on adiposity measures in adults.

### Keywords

vitamin D; adiposity; supplementation

## Introduction

Obesity is one of the greatest causes of preventable morbidity and mortality worldwide[1] and coexists with vitamin D insufficiency.[2] Given the increasing rates of obesity[1] across many populations worldwide, finding strategies to curb this epidemic is of critical public health importance. Obesity augments risk of cardiovascular disease (CVD), type 2 diabetes, and many other chronic diseases. As an essential fat-soluble vitamin that is stored in adipose tissue,[3,4] the role of vitamin D in the pathogenesis of obesity and chronic diseases is an area of tremendous importance to clinical nutrition and public health.

A bidirectional relationship exists between obesity and vitamin D metabolism and storage.[3] Observational studies have reported an increased risk of vitamin D deficiency in obese individuals, but the direction of causality and the underlying mechanisms are unclear.[4] The larger storage capacity for vitamin D in obese individuals by fat sequestration[3] or volumetric dilution[5] may result in lower plasma vitamin D. Furthermore, there has been recent debate about what constitutes vitamin D deficiency and sufficiency.[6] The most recent compilation of data suggest 25-hydroxyvitamin D(25(OH)D)level of 50 nmol/L (20 ng/ml) is adequate for the population. However, the 2011 Institute of Medicine (IOM) report concluded that there is currently only sufficient evidence to provide health guidelines for skeletal health, that more data are needed on non-skeletal outcomes as well as to identify the threshold effects for other health outcomes.[7,8]

Clarity is required in understanding the inverse relationship of vitamin D and measures of body fatness. By reverse causation, prevention of obesity may improve vitamin D status.[9] Possible anti-obesity mechanisms of calcium and vitamin D include the control of adipocyte death, adipogenesis, and lipid metabolism.[10] Observational studies have suggested that sufficient vitamin D status (25(OH)D ≥ 50 nmol/L is associated with a reduced risk of diseases that cluster with obesity such as cardiovascular disease, diabetes, and certain cancers.[11,12] Vitamin D supplements may interact with calcium and parathyroid hormone (PTH) to affect adiposity.[2] Elevated PTH related to low serum 25(OH)D concentration (25(OH)D < 50 nmol/L) might affect calcium influx into adipose cells and promote weight gain.[13] The active vitamin D metabolite 1,25 dihydroxyvitamin D3 may also modulate adipogenesis independent of PTH.[14] A recent animal study reported a lower gain in weight in mice fed a high fat diet with calcium and vitamin D compared to the high fat diet alone.[15]

Animal studies on vitamin D receptor (VDR) null mice suggest a role for vitamin D in energy regulation.[16]

Human observations since the 1980s of lower levels of 25(OH)D in obese than in nonobese individuals highlight a possible inverse relation between vitamin D and obesity.[17] Cross-sectional studies have shown an inverse association between 25(OH)D levels and adiposity assessed by various measures.[18,19] This significant association has not been shown in all studies.[20-22]

Similarly, conflicting results have been reported regarding the association of directly measured total fat with 25(OH)D versus other anthropometric measures.[19] For example, Moschonis et al. observed significant associations between vitamin D levels and body composition indices, measured by dual-energy x-ray absorptiometry (DXA), but no significant associations between anthropometric indices of body mass and vitamin D levels.[21] Another study suggests that anthropometric measures and directly measured total fat by DXA were inversely associated with 25(OH)D.[19]

These observational results suggest that improving vitamin D status may be an effective intervention for obesity prevention and management. Few intervention trials were specifically designed to evaluate the direct effects of vitamin D supplementation on adiposity measures, and existing trials with adiposity as a secondary outcome have produced conflicting results. Some trials showed no association of vitamin D supplementation with weight loss[23,24] while others showed potential benefits that may be dependent on adjunctive calcium supplementation.[25,26] Choice of adiposity measures may be important in the evaluation of relationships between vitamin D supplementation and adiposity.[27] Only a few trials of vitamin D have assessed changes in body composition or in visceral or other fat depots, as directly measured by DXA,[23,28,29] magnetic resonance imaging (MRI), or computed tomography (CT).[30,31] DXA provides measures of overall adiposity, lean tissue, and regional distributions, with good reproducibility and minimal radiation exposure.[32,33] Adequately powered RCTs with direct assessments of adiposity, such as DXA, are warranted to clarify the direct effect of vitamin D with or without calcium on adiposity.

A recent meta-analysis assessing the effect of only vitamin D supplementation on adiposity measures reported null results, but an effect by vitamin D dose was not evaluated.[34] We therefore conducted a meta-analysis of randomized controlled trials to quantitatively assess dose effects of vitamin D supplementation alone or in combination with calcium on changes in three widely used adiposity measures, including body weight, body mass index (BMI), or fat mass (FM).

## METHODS

### Data Sources and Literature Search

Based on our hypothesis that vitamin D supplementation alone or with calcium alters adiposity measures, we developed and followed a standard protocol for this literature review and meta-analysis (Figure 1). PICOS (participants, interventions, comparators, outcomes, and study design) criteria are listed in Table 1. We searched published literature on

MEDLINE, EMBASE, and Cochrane Central Register of Controlled Trials from 1966 to March 2014. The search terms were selected to capture generic and specific words relevant to the exposure and outcome on the basis of Medical Subject Heading (MeSH) terms and text key words from a priori identified articles. Terms selected for vitamin D included vitamin D intake, vitamin D supplement, calcidiol, calcitriol, cholecalciferol (vitamin D3), and ergocalciferol (vitamin D2). Terms for adiposity included overweight, weight loss, BMI, body mass index, adipose tissue, fat mass, or body fat distribution. We restricted the search to articles published in English and studies of human subjects aged 18 years or older and applied the same search strategy to each database. We also manually searched reference lists of retrieved articles for additional studies. Details of our literature search are available in the Appendix. All vitamin D data were converted as necessary to international units (IU) per day for intake (except for the Ljunghall study[21] which used alphacalcidiol which does not have an IU conversion or dose approximation to vitamin D3 or vitamin D2) and $nmolL^{-1}$ for 25(OH)D status.

## Study Selection

Two independent investigators (P.D.C. and X.Z.) assessed each abstract and article according to inclusion criteria and critically evaluated the methodological quality. Study selection was limited to randomized, double-blind, controlled trials that had a minimum of 50 participants, minimum duration of intervention for 3 months, and measurement of BMI, body weight, or FM (Table 1). Fifty participants is generally accepted as the minimum number required for adequate power for correlation or regression models.[35] A minimum three month intervention period allows for adequate time to assess changes in adiposity measures.[36] Maximum weight loss from pharmacologic[37,38] and behavioral interventions[39,40] usually peaks around 6 months. Short-term efficacy is a suboptimal endpoint because recidivism is common when anti-obesity medications are stopped.[36] One-third to two-thirds of the weight loss is regained within one year and almost all is regained within 5 years.[40,41] We used these adiposity outcome measures, because they are commonly reported measures. We did not include waist circumference (WC) as an adiposity outcome, because we had two few studies[23,27,42,43] included in this meta-analysis with available information for a meaningful analysis. The primary method used to measure fat mass in the included studies was DXA, but different fat mass values were reported including truncal fat, whole body fat, and body fat percentage. Bioelectrical impedance analysis (BIA) was used in one study.[43] Caloric restriction or changes in background diet were a parallel focus in three studies included in this meta-analysis.[43-45] If baseline and end of study values were not reported for BMI, weight, or FM, we contacted authors for additional information. We excluded studies of children and adolescents and studies that did not assess use of vitamin D supplements, with or without combination of calcium, based on abstract review. We retrieved articles that passed abstract screening for a full-text review and further excluded studies involving patients with chronic diseases such as cancer, end stage renal disease, and inflammatory bowel disease, which may have induced pathologic changes in adiposity.

## Assessment of Methodological Quality

Two investigators (P.D.C. and X.Z.) reviewed and extracted data of study design, participant characteristics, interventions, and outcomes. We assessed the methodological quality of each

included trial by using the Jadad score.[46] The domains used in the present meta-analysis pertained to randomization and allocation concealment (selection bias), blinding (performance and detection bias), and loss to follow-up and adherence to the intention-to-treat principle (attrition bias). We present all studies and provided a summary score for the study quality assessment across studies. Two measures were used to estimate fat mass, dual-energy X-ray absorptiometry (DXA) and BIA.

### Statistical Analyses

We analyzed studies with vitamin D alone supplementation versus placebo, vitamin D plus calcium supplementation versus calcium control-which is a test of vitamin D, and vitamin D plus calcium supplementation versus placebo. Most of these studies reported more than one adiposity outcome. To investigate the dose-response effect, subgroup analyses stratified by vitamin D dose were performed. In each of these subgroup analyses, each study contributed only one dose category, except for one study.[47]

We used the DerSimonian-Laird random-effects model to examine the effects of vitamin D with or without calcium supplements on adiposity measurements. We calculated the weighted mean differences (95% CI) based on the random-effects model. Heterogeneity between trials was assessed using Chi-square statistic with the significance level set at $P<0.05$. We also quantified the extent of heterogeneity with the $I^2$ value, where the percentages of $I^2$ 25-50%, 50-75%, and >75% indicate low, medium, and high heterogeneity, respectively.[48] To examine whether the summary estimates were robust to the results from individual studies, pre-specified sensitivity analyses were employed by repeating the analysis with the study with the largest effect removed. In a meta-analysis, the heterogeneous nature of the pooled meta-analysis results may present a challenge for validity and interpretation of any quantitiative synthesis.[49] To understand major sources of heterogeneity, we performed sensitivity analyses with and without the major source of heterogeneity (identified as the study with the largest effect) to assess the robustness of the pooled estimates. Analyses were conducted using Stata SE 13 software (StataCorp, College Station, Texas). All *P* values were 2-tailed, and a *P* value less than 0.05 was considered to indicate a significant difference.

## Results

From the literature search, a total of 953 studies were identified through electronic database search and 2 through manual search. **Figure 1** shows the summary results from literature search and study selection. Twenty-six RCTs met our inclusion criteria, providing data on 42,430 participants with median treatment duration of 12 months. We obtained study summary data directly from the authors for 10 studies.[50-59] All studies reported adequate randomization and blinding of study data to data collectors and outcome assessors. Studies had a Jadad score of 3-5. Among 26 studies included in this meta-analysis, 24 reported BMI as an outcome, 13 reported FM as an outcome, and 21 reported weight as an outcome. Overall, the median [interquartile] duration of treatment was 12 [6, 36] months, the baseline BMI was 29.3 [27.5, 32.1] kg/m$^2$, and the baseline age was 60.6 [48.8, 68.0] years. All studies used vitamin D3, except one that used vitamin D2 [60], and another used

alphacalcidiol.[61] **Table 2**28, 42, 43, 45, 61, 62, 63, 64, 53, 58, 65, 51, 23, 26, 66, 67, 68, 54, 59, 55, 60, 50, 44, 69, 70, 56 provides an overview of the number of participants, methodological quality, and the baseline and end of intervention values of weight, BMI, or FM in each included trial. Twenty-five studies reported no significant effect of vitamin D alone or vitamin D plus calcium supplementation on weight, BMI, or FM. Seven studies examined change in weight, BMI, or FM as the primary outcome.

Vitamin D supplementation alone versus placebo resulted in no significant change in BMI, weight, or FM.(**Table 3**) Vitamin D plus calcium supplementation versus calcium also showed no significant reduction in BMI, weight, or FM.(**Table 3**) Together, vitamin D alone versus placebo and vitamin D plus calcium versus calcium control showed no significant reduction in BMI, weight, or FM. (**Table 3; Supplemental Figures 1-3** 42, 43, 45, 61, 62, 63, 64, 53, 58, 65, 51, 23, 26, 66, 67, 68, 54, 59, 55, 60, 50) An analysis for dose-response effect by vitamin D3 dose of < 1000, 1000 to < 2000, 2000 to < 4000, and greater than 4000 IU/day (**Figures 2a-2c** 42, 43, 45, 61, 62, 63, 64, 53, 58, 65, 51, 23, 26, 66, 67, 68, 54, 59, 55, 60, 50,) revealed no significant effect of vitamin D in any of the dose groups on any of the adiposity outcomes ( all $p>0.05$). The highest daily dose in the studies included in this meta-analysis was vitamin D3, 12,695 IU/day.[53] With a limited number of eligible trials, vitamin D plus calcium versus placebo showed no significant reduction in BMI and FM, but a significant reduction in body weight.(**Table 3**) In sensitivity analysis, the significant result for weight was largely driven by the inclusion of a single trial with only the weight estimate available, the Women's Health Initiative (WHI) vitamin D/calcium trial.[44](Table 3) This trial reported the largest and most significant effect on weight. Weight change was not significantly different for vitamin D plus calcium compared with placebo after excluding this WHI trial. (**Table 3; Supplemental Figures 4-7**[44, 69, 70, 56])

Neither Begg's test nor Egger's test were significant for publication bias in the major effects of vitamin D with or without calcium supplements on BMI, weight, or FM.

## Discussion

The possible role of vitamin D in the pathogenesis of obesity[71,72] is an area of importance to public health and clinical nutrition given the suboptimal vitamin D status across many populations worldwide[73] and the soaring global prevalence of obesity.[1] There is lack of knowledge currently to guide dietary recommendations for vitamin D intake in relationship to adiposity. The IOM definition of vitamin D inadequacy (25(OH)D < 50 nmol/L) is predominantly derived from bone health outcomes and is evolving.[7,8] How achieved levels vary by BMI and total and regional fat (ex. abdominal) is understudied, with little known about the dynamics of vitamin D storage and reentry into the circulation.[74]

The conventional explanation for low vitamin D in obese individuals is that the volume of distribution for this fat-soluble vitamin is larger in patients with excess fat.[3] We postulated that the obesity is a result of the low vitamin D. The results of this meta-analysis of 26 RCTs showed no overall evidence for significant effects of vitamin D or vitamin D plus calcium supplementation on BMI, weight, or FM. There was no evidence for a dose-response effect from our analyses stratified by vitamin D dosages even though the baseline BMI (median

29.3 kg/m$^2$) of the overall study population was nearly at the threshold for obesity. This analysis was conducted in adults and may not be generalizable to other groups.

The trials of vitamin D alone versus placebo and of vitamin D plus calcium versus calcium are clear tests of vitamin D, whereas the comparison of Vitamin D plus calcium to placebo assesses the combined effect of vitamin D and calcium. The vitamin D plus calcium versus placebo pooled result was not robust to the inclusion and exclusion of the WHI vitamin D/calcium trial, arguing against the possibility of a genuine effect.[25] The WHI vitamin D/calcium trial was imbedded in the other WHI RCTs, including a diet modification trial that may have led to weight loss, thus influencing the effects of combined vitamin D/calcium supplementation.

In any meta-analysis, the heterogeneous nature of the pooled meta-analysis results presents a challenge for interpretation of any quantitative synthesis. In the present study, we have followed the pre-specified inclusion/exclusion criteria when combining the results from all eligible studies, including the WHI. However, the WHI results predominantly contributed to between-study heterogeneity. To understand such a major source of heterogeneity, we performed sensitivity-analyses with and without the WHI to assess the robustness of the pooled estimates.

The number of subjects included in this meta-analysis is small compared to the number of subjects who have participated in clinical trials of vitamin D because study selection criteria included only randomized double blind placebo controlled clinical trials of at least 3 months of treatment. These selection criteria resulted in a 12-month median duration of treatment for robust assessment of weight loss.[36,37]

The observed significant heterogeneity for FM outcomes may have been influenced by the variety of FM measures reported or age of study participants. Although all studies in this meta-analysis used DXA, with the exception of one study that used BIA,[43] FM outcomes included truncal fat, whole body fat, and body fat percentage. Fat mass heterogeneity may also have been influenced by age since the study with the greatest reduction in FM for the vitamin D only group was Salehpour et al.[27] (mean age 38), where as the other studies had older participants. FM increases with age.[75,76-79]

Our results highlight the need for intervention studies of sufficient size to help clarify the relationship between vitamin D and adiposity as affirmed in the IOM report.[7,8] Objective assessments of adiposity including measures of fat mass (total and regional) using gold standard methods, such as DXA, are warranted. DXA provides measures of total body weight, overall adiposity and regional distributions, non-fat-containing tissues (lean and bone mass), with good reproducibility and minimal radiation exposure.[32,33] The VITamin D and OmegA-3 TriaL (VITAL) is a double-blind, placebo-controlled trial assessing the role of the interventions (vitamin D3, 2000 IU/day and omega-3 fatty acid, 1 g/day) in reducing risks of cancer and cardiovascular disease among U.S. men and women. An ancillary VITAL study will comprehensively test effects of supplemental vitamin D and/or omega-3 on skeletal health by using DXA scans to assess changes in bone and body composition with vitamin D and omega-3 fatty acid supplementation.[80] Results from VITAL will help clarify

the relationship between supplemental vitamin D and adiposity outcomes, and inform clinical care and public health guidelines on the use of supplemental vitamin D in obese individuals.

Observational studies show lower levels of 25(OH)D in obese than in nonobese individuals, suggesting a possible beneficial effect of vitamin D on obesity.[17] A study of community dwelling participants suggested that almost all the variability in serum 25(OH)D concentrations was attributable to obesity.[5] Once serum 25(OH)D concentrations were adjusted by body size, there was no longer a difference between obese and non-obese participants.[5] Few intervention trials have been specifically designed to evaluate the direct effects of vitamin D on adiposity measures and have produced conflicting results. Results of some RCTs suggested beneficial effects of vitamin D supplementation[2581] on body weight regulation but others did not.[23,26] A systematic review[2] of five RCTs[23,43,62,82,83] found that vitamin D supplementation did not promote weight or fat loss. A recent meta-analysis with 12 studies found no significant effect of only vitamin D supplementation on adiposity measures, but an effect by vitamin D dose was not evaluated.[34] A bidirectional genetic study suggested that higher BMI results in lower 25(OH)D, but the effects of lower 25(OH)D on BMI are likely to be small.[84] In addition, despite plausible mechanisms and in vitro evidence[14,16] supporting a role for vitamin D in weight reduction, it remains difficult to determine whether the effects are due to vitamin D itself or are related to calcium that is usually consumed in combination.

Our overall results may be explained by multiple reasons. First, it is possible that there is no biological effect of supplementation with vitamin D, with or without calcium, on adiposity. Second, clinical trials that evaluated the effect of vitamin D and calcium on measures of adiposity varied by study design. The published studies differ substantially in terms of methodology including participant recruitment and intervention, making it difficult to pool the findings. For example, some studies that showed no effect of vitamin D supplementation on weight recruited participants who were vitamin D replete. The results may not apply to individuals who were vitamin D insufficient. There has been recent debate about what constitutes vitamin D deficiency and sufficiency[6]; thresholds have recently shifted. The most recent compilation of data suggests 25(OH)D levels of 50 nmol/L (20 ng/ml) are adequate for the population. However, the 2011 IOM report concluded that there is currently only sufficient evidence to provide health guidelines for skeletal health, that more data are needed on non-skeletal outcomes as well as to identify the threshold effects for other health outcomes.[7,8]

Third, the choice of adiposity measure[85] is important in the evaluation of the relation between vitamin D supplementation and adiposity. A limitation of anthropometric measures, such as BMI or weight, is that they do not separate fat from lean mass and are unable to characterize the type and distribution of fat deposits (e.g. intramyocellular, subcutaneous, or visceral).[86] Lipids stored in other tissue, such as liver and muscle, also contribute to the adipose compartment.[87,88] Anthropometric measurements such as subscapular and triceps skinfold thickness, waist circumference, and waist to hip ratio allow for indirect assessment of fat distribution.[89] Similarly, DXA, a noninvasive method for measuring regional fat mass, cannot differentiate between visceral, subcutaneous, and intramyocellular fat.[90] In contrast,

CT and MRI allow precise quantification of visceral adipose tissue and subcutaneous adipose tissue. [86] Similarly, magnetic resonance spectroscopy (MRS) can measure fat in other tissues such as muscle and liver.[91] Thus, this analysis omits a variety of measures of adiposity.

Due to limited data, our analysis did not examine regional adipose tissue distribution or waist circumference. Cross-sectional and observational studies provide evidence of inverse association between 25(OH)D levels and obesity, and in some instances, fat mass, fat distribution, and anthropomorphic measures.[3,17,19,92-99] This relationship, however, was not evident in all studies.[100,101] Fourth, the older age of the participants (median age 60.6 years) may have influenced our findings. At the same body weight level, FM distribution differs by age, sex, and fitness.[75] Body composition changes associated with aging, include increase in FM in mid to early old age[75,76-79] and loss of fat-free mass (FFM),[77,102] including muscle and bone.[78,79,102,103] Furthermore, vitamin D insufficiency may not have been corrected with vitamin D supplementation since markedly higher proportions of insufficient vitamin D levels have been reported among elderly adults.[104-109]

Next, the quality of our studies was limited by small sample size and short duration of some trials. Our literature search identified only 8 studies with small sample size that evaluated the effect of vitamin D alone or vitamin D plus calcium (with calcium control) on FM and the meta-analysis showed no effect of vitamin D supplementation. In all but two studies, body composition was measured by DXA, a high quality method. Yet, a recent review of 15 RCTs evaluated the potential role of calcium and vitamin D in the regulation of body weight or body fat also found no overall effect of vitamin D and calcium on body weight or body fat.[110]

Alternatively, vitamin D and calcium deficiency may have important latent effects. Inadequate intake of nutrients contributes to many chronic diseases that take years to manifest themselves. Thus, calcium and vitamin D may have short- and long-term effects in the development of obesity.[111] The vitamin D and calcium intake required to prevent the long-latency chronic disorders may be higher than those required to prevent developmental problems such as rickets. However, whether these actions of vitamin D are important enough to result in obesity in D-deficient individuals is doubtful. The negative result of this study suggests that vitamin D supplementation will not be helpful in reducing obesity.

Some limitations of our analysis deserve consideration, including the inability to conduct robust subgroup analyses based on duration of intervention, baseline 25(OH)D concentration, baseline BMI or baseline waist circumference. We could not evaluate whether different formulations of vitamin D, such as vitamin D2, have different effects on adiposity measures because most of the studies used vitamin D3. Furthermore we did not evaluate the influence of seasonality on vitamin D response to supplementation. Importantly, we did stratify by vitamin D dose and observed no signal of a dose-responsive trend for effect of vitamin D on BMI or weight. Several important factors may confound a relationship between vitamin D status and obesity. The first is behavioral. Obese people may be less likely to expose themselves to sunshine.

In patients who are truly vitamin D deficient, replacement with vitamin D improves the bone density which will increase the lean tissue mass. This could mask a beneficial effect on fat mass if body weight is the only outcome measurement.

In conclusion, our meta-analysis of RCTs showed no overall evidence for direct effects of vitamin D on BMI, weight, or FM as measures of adiposity. Fat mass and fat distribution are more meaningful measures of adiposity than body weight and BMI. Yet, the former two were only reported as outcomes in a minority of the included RCTs. Our robust findings are directly relevant to public health and clinical nutrition and corroborate and support the advancement of vitamin D research on the relationship between vitamin D and obesity. There is a clear need for adequately powered RCTs that include the assessment of baseline 25(OH)D and objective measures of obesity using gold standard methods such as DXA.

## Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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## Abbreviations

| | |
|---|---|
| **BMD** | bone mineral density |
| **Wt** | weight |
| **FM** | fat mass |
| **BMI** | body mass index |
| **FFM** | fat free mass |
| **BIA** | Bioelectrical impedance analysis |
| **CI** | confidence interval |

| | |
|---|---|
| **WMD** | weighted mean difference |
| **RCT** | randomized clinical trial |
| **PTH** | parathyroid hormone |
| **25(OH)D** | dual-energy X-ray absorptiometry |
| **MRI** | magnetic resonance imaging |
| **MRS** | magnetic resonance spectroscopy |
| **CT** | computed tomography |
| **IU/d** | international units/day |
| **mg/d** | milligrams/day |
| **ug/day** | micrograms/day |
| **nmol/L** | nanomole/liter |
| **MeSH** | Medical Subject Headings |
| **IOM** | Institute of Medicine |
| **Vitamin D2** | ergocholecalciferol |
| **Vitamin D3** | cholecalciferol |

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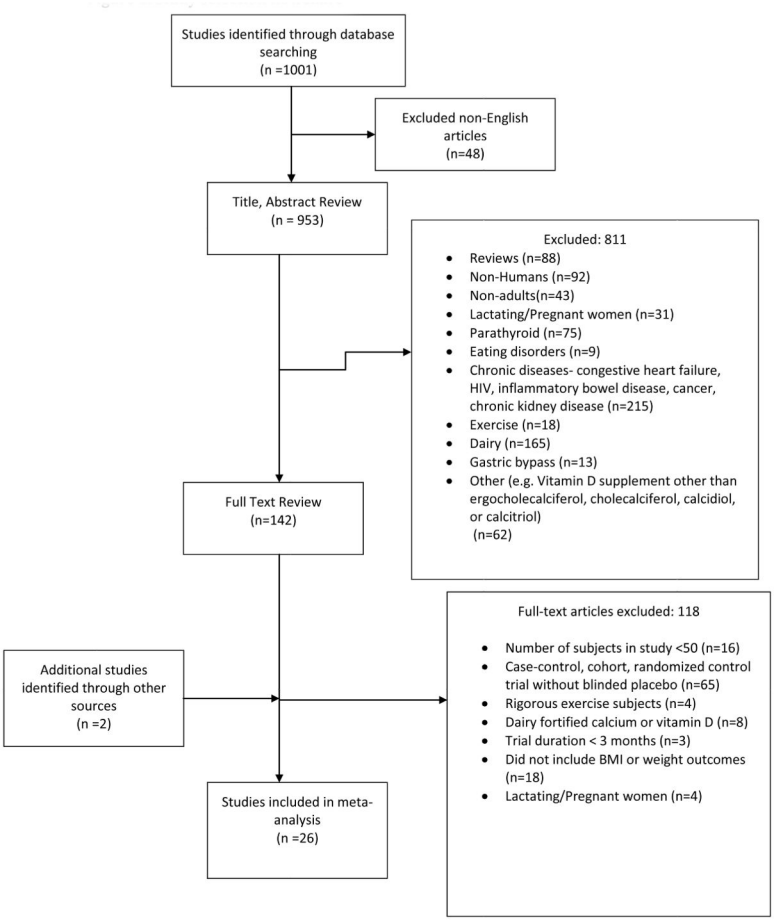
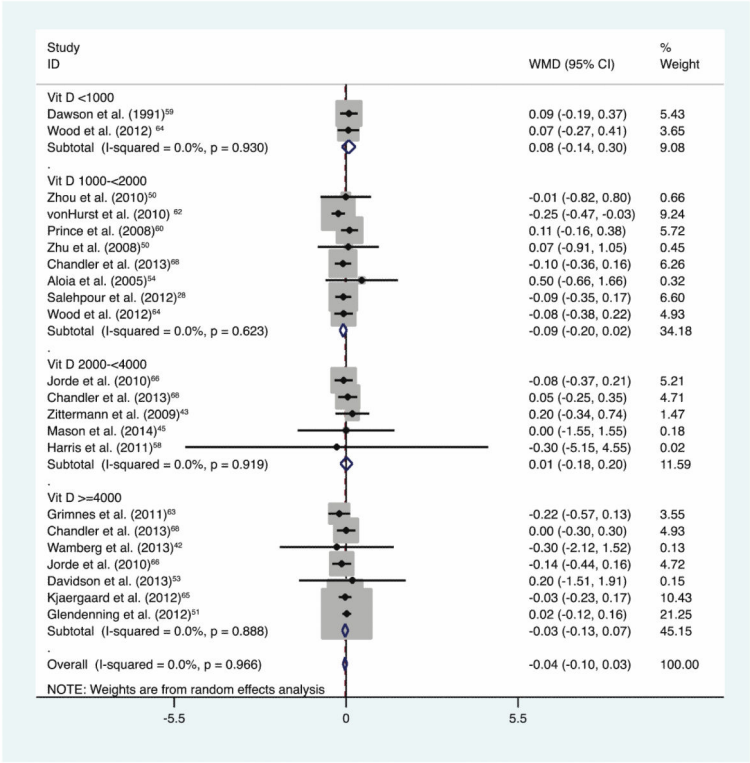
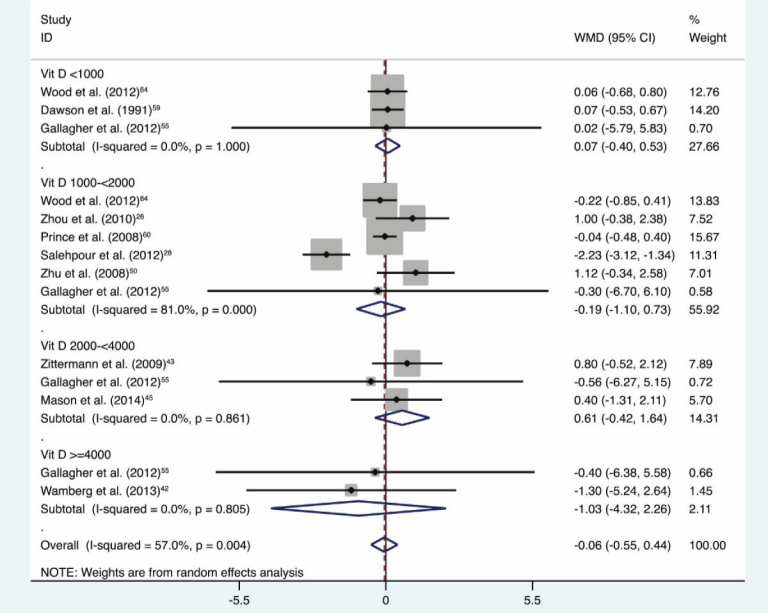



**Figure 1.**
Study selection flowchart



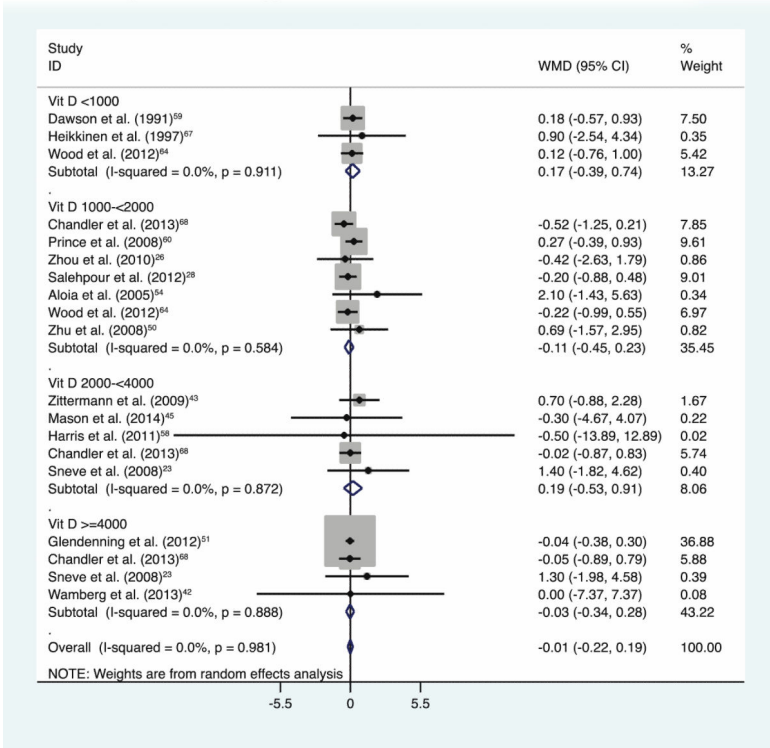



**Figure 2.**

Dose effect comparisons for vitamin D alone supplementation versus placebo and vitamin D plus calcium supplementation versus calcium control for BMI (**2a**), weight (**2b**), and FM (**2c**)

## Table 1

PICOS (participants, interventions, comparators, outcomes, and study design) criteria

| **Does the use of vitamin D supplementation alone or with calcium change adiposity measures?*** | | | | |
|---|---|---|---|---|
| **Population** | **Intervention** | **Comparator** | **Outcome** | **Setting** |
| General adult population | Supplementation with vitamin D alone | Placebo | Change in adiposity measures (BMI, FM, and weight) | Randomized, double-blind, controlled trials with a minimum of 50 participants, minimum intervention duration of 3 months, and measurement of BMI, FM, and weight |
| General adult population | Supplementation with vitamin D and calcium | Calcium | Change in adiposity measures (BMI, FM, and weight) | Randomized, double-blind, controlled trials with a minimum of 50 participants, minimum intervention duration of 3 months, and measurement of BMI, FM, and weight |

*Abbreviations: BMI, body mass index in $kg/m^2$; FM, fat mass

**Table 2**

Characteristics of randomized controlled trials selected for the meta-analysis[a]

| Source/Year/Country /Jadad Score[b] | Treatment Group | Subjects, No. | Duration (months) | Age, years[a] Mean (SD) | Men,n (%) | Baseline 25(OH)D, nmol/l[a,g] | VitaminD (IU/d)/ Calcium (mg/d)[d] | Adiposity Measure | Baseline | End of Study[f] | Outcome |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **Vitamin D alone** | | | | | | | | | | | |
| **Salehpour et al. (2012)[28] Iran, 4** | D3 | 42 | 3 | 38(7) | 0 | 36.8 (30) | 1000/− | BMI | 30.1 (3.9) | 30 (4) | Adiposity |
| | | | | | | | | Wt | 73.9 (10.2) | 75.1 (11.9) | |
| | | | | | | | | FM | 30.2 (6.9) | 28.2 (7.5) | |
| | Placebo | 43 | | 37 (8) | 0 | 46.9 (32) | | BMI | 29.5 (4.4) | 29.5 (4.6) | |
| | | | | | | | | Wt | 73.5 (10.4) | 75 (12.3) | |
| | | | | | | | | FM | 29.0 (8.7) | 28.6 (8.9) | |
| **Wamberg et al. (2013)[42] Denmark, 5** | D3 | 26 | 6.5 | 39.5 (8.0) | 8 (30.8) | 34.5 (10.8) | 7000/− | BMI | 36.3 (3.5) | 36.4 (3.5) | Adiposity |
| | | | | | | | | Wt | 105 (14) | 105 (13) | |
| | | | | | | | | FM | 40.2 (8.1) | 41.8 (7.6) | |
| | Placebo | 26 | | 41.2 (6.8) | 7 (26.9) | 34.6 (10.3) | | BMI | 34.8 (3.3) | 34.6 (3.0) | |
| | | | | | | | | Wt | 100 (13) | 100 (14) | |
| | | | | | | | | FM | 37.4 (6.5) | 37.7 (6.6) | |
| **Zittermann et al. (2009)[43] Germany, 3** | D3 | 100 | 12 | 47.4 (10.3) | 31 (37.8) | 30.0 (17.5) | 3332/− | BMI | 33.7 (4.1) | 31.8 (4.8) | Adiposity in a weight loss program |
| | | | | | | | | Wt | 101.9 (16.1) | 96.1 (15.0) | |
| | | | | | | | | FM | 40.1 (10.2) | 35.9 (11.1) | |
| | Placebo | 100 | | 48.8 (10.1) | 23 (27.7) | 30.3 (20.1) | | BMI | 33.0 (4.3) | 30.9 (4.6) | |
| | | | | | | | | Wt | 96.2 (17.4) | 89.7 (14.5) | |

| Source/Year/Country /Jadad Score[b] | Treatment Group | Subjects, No. | Duration (months) | Age, years[a] Mean (SD) | Men,n (%) | Baseline 25(OH)D, nmol/l[a,g] | VitaminD (IU/d)/ Calcium (mg/d)[d] | Adiposity Measure | Baseline | End of Study[f] | Outcome |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | FM | 38.5 (9.9) | 33.5 (9.5) | |
| **Mason et al. (2014)[45] USA, 5** | D3 | 109 | 12 | 60.3 (5.3) | 0 | 53.3 (15.2) | 2000/− | BMI | 32.3 (5.5) | 29.5 (5.6) | Adiposity in a weight loss program |
| | | | | | | | | Wt | 87.4 (15.5) | 80.2 (15.6) | |
| | | | | | | | | FM | 23.7 (6.2) | 19.6 (6.6) | |
| | Placebo | 109 | | 59.0 (4.7) | 0 | 53.3 (15.4) | | BMI | 32.5 (6.1) | 29.7 (6.1) | |
| | | | | | | | | Wt | 88.1 (17.1) | 80.7 (17.6) | |
| | | | | | | | | FM | 24.2 (6.0) | 20.5 (6.9) | |
| **Ljunghall et al. (1987)[61] Scandinavia, 3** | Vitamin D (alphacalcidiol) | 33 | 3 | 61-65[c] | 100 | 92.4 (23.5) | 0.75 ug /− | BMI | 27.5 (3.4) | 27.2 (3.2) | Insulin secretion |
| | | | | | | | | Wt | 85.7 (12.8) | 84.6 (12.4) | |
| | Placebo | 32 | | 61-65 | 100 | 97.3 (72.4) | | BMI | 28.2 (4.0) | 28.1 (3.9) | |
| | | | | | | | | Wt | 87.6 (13.7) | 87.5 (13.5) | |
| **Von Hurst et al. (2010)[62] New Zealand, 3** | D3 | 42 | 6 | 41.8 (10.1) | 0 | 21 [11,40] | 4000/− | BMI | 27.5 (5.0) | N/A[f] | Insulin Resistance |
| | Placebo | 39 | | 41.5 (9.1) | 0 | 19 [13,29] | | BMI | 27.4 (3.7) | N/A[f] | |
| **Grimnes et al. (2011)[63] Norway, 5** | D3 | 51 | 6 | 51.5 (8.8) | 27 (55) | 42.2 (13.9) | 5714/− | BMI | 27.2 (3.1) | 26.8 (3.2) | Insulin sensitivity |
| | Placebo | 53 | | 52.7 (9.7) | 22 (49) | 39.2 (12.1) | | BMI | 26.3 (2.9) | 26.2 (2.8) | |
| **Wood et al. (2012)[64] UK, 5** | D3 | 102 | 12 | 63.5 (1.9) | 0 | 32.7 (12.9) | 400/− | BMI | 26.6 (4.2) | 26.4 (3.9) | Serum lipid profile, insulin resistance, inflammatory biomarkers |
| | | | | | | | | Wt | 68.6 (12.7) | 68.1 (12.1) | |
| | | | | | | | | FM | 27.9 (8.1) | 27.6 (8.2) | |

| Source/Year/Country /Jadad Score[b] | Treatment Group | Subjects, No. | Duration (months) | Age, years[a] Mean (SD) | Men,n (%) | Baseline 25(OH)D, nmol/l [a,g] | VitaminD (IU/d)/ Calcium (mg/d)[d] | Adiposity Measure | Baseline | End of Study[f] | Outcome |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | D3 | 101 | | 64.1 (2.3) | 0 | 32.4 (13.8) | 1000/− | BMI | 26.8 (4.2) | 26.8 (4.2) | |
| | | | | | | | | Wt | 69.6 (11.9) | 69.8 (12.0) | |
| | | | | | | | | FM | 27.9 (8.1) | 28.3 (8.5) | |
| | Placebo | 102 | | 63.9 (2.3) | 0 | 36.2 (17.1) | | BMI | 26.6 (4.4) | 26.9 (4.4) | |
| | | | | | | | | Wt | 69.3 (12.5) | 70.3 (12.3) | |
| | | | | | | | | FM | 27.7 (8.3) | 28.5 (8.7) | |
| **Davidson et al. (2013)[53] USA, 4** | D3 | 56 | 12 | 52.3 (8.0) | 20 (36) | 54.9 (11.2) | 12695/− | BMI | 32.1 (4.7) | 32.6 (4.5) | Insulin secretion and sensitivity |
| | Placebo | 53 | | 52.5 (7.0) | 15 (29) | 54.9 (11.9) | | BMI | 32.9 (4.3) | 31.6 (4.7) | |
| **Harris et al. (2011)[58] USA, 3** | D3 | 23 | 4 | 29 (2) | 9 (41) | 34.3 (2.2) | 2000/− | BMI | 30.4 (8.6) | 30.5 (8.7) | Flow Mediated |
| | | | | | | | | Wt | 87.2 (24.3) | 85.5 (20.8) | Dilation |
| | Placebo | 21 | | 31 (2) | 12 (52) | 38.2 (3.0) | | BMI | 29.1 (7.4) | 28.9 (7.9) | |
| | | | | | | | | Wt | 87.1 (24.0) | 84.9 (21.5) | |
| **Kjaergaard et al. (2012)[65] Norway, 4** | D3 | 120 | 6 | 53.4 (10.3) | 54 (45) | 47.4 (15.8) | 5714/− | BMI | 27.5 (4.0) | 28.0 (4.2) | Depressive symptoms |
| | Placebo | 110 | | 53.3 (10.1) | 47 (42.7) | 47.7 (15.5) | | BMI | 27.5 (4.0) | 28.0 (4.3) | |
| **Glendenning et al. (2012)[51] Australia, 5** | D3 | 353 | 9 | 76.9 (4.0) | 0 | 65.0 (17.8) | 5000/− | BMI | 27.41 (4.7) | 27.39 (4.91) | Falls, muscle strength, and mobility |
| | | | | | | | | Wt | 70.61 (13.0) | 70.19 (13.4) | |
| | Placebo | 333 | | 76.5 (4.0) | 0 | 66.5 (27.1) | | BMI | 27.24 (4.8) | 27.19 (4.69) | |
| | | | | | | | | Wt | 70.48 (12.89) | 70.10 (12.66) | |
| **Vitamin D and Calcium versus Calcium Control** | | | | | | | | | | | |
| **Sneve et al. (2008)[23] Norway, 3** | | 153 | 12 | 46.4 (11.3) | 57 (37.2) | 54.5 (16.7) | 5714/500 | BMI | 35.0 (4.1) | N/A | Adiposity |

| Source/Year/Country /Jadad Score[b] | Treatment Group | Subjects, No. | Duration (months) | Age, years[a] Mean (SD) | Men,n (%) | Baseline 25(OH)D, nmol/l[a,g] | VitaminD (IU/d)/ Calcium (mg/d)[d] | Adiposity Measure | Baseline | End of Study[f] | Outcome |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | D3/Calcium | | | | | | | | | | |
| | | | | | | | | Wt | 101.0 (14.5) | 100.3 (14.9) | |
| | | | | | | | | FM | 42.9 (7.9) | N/A | |
| | | 143 | | 47.6 (11.9) | 51 (35.7) | 51.4 (18.4) | 2857/500 | BMI | 34.4 (3.9) | N/A | |
| | D3/Calcium | | | | | | | | | | |
| | | | | | | | | Wt | 98.6 (14.3) | 97.8 (13.3) | |
| | | | | | | | | FM | 42.9 (7.6) | N/A | |
| | Calcium | 149 | | 48.9 (11.0) | 51 (34.2) | 53.2 (15.4) | −/500 | BMI | 35.1 (3.8) | N/A | |
| | | | | | | | | Wt | 100.6 (13.9) | 101.2 (14.6) | |
| | | | | | | | | FM | 43.1 (6.9) | N/A | |
| **Zhou et al. (2010)[26] USA, 4** | D3/Calcium | 336 | 48 | 66.5 (7.5) | 0 | 73.1 (18.8) | 1100/1400-1500 | BMI | 28.7 (5.2) | 28.2 (5.2) | Adiposity |
| | | | | | | | | Wt | 75.5 (14.3) | 73.4 (14.5) | |
| | | | | | | | | FM | 29.8 (8.7) | 29.2 (9.3) | |
| | Placebo | 206 | | 65.2 (6.5) | 0 | 73.6 (20.7) | | BMI | 28.8 (5.3) | 28.7 (5.5) | |
| | | | | | | | | Wt | 76.4 (14.2) | 75.8 (14.3) | |
| | | | | | | | | FM | 30.1 (9) | 30.5 (9.2) | |
| | Placebo/ Calcium | 328 | | 66.0 (6.6) | 0 | 73.0 (20.4) | −/1400-1500 | BMI | 28.9 (5.4) | 28.7 (5.4) | |
| | | | | | | | | Wt | 76.6 (14.8) | 74.4 (14.4) | |
| | | | | | | | | FM | 30.7 (9.2) | 29.7 (9.0) | |

| Source/Year/Country /Jadad Score[b] | Treatment Group | Subjects, No. | Duration (months) | Age, years[a] Mean (SD) | Men,n (%) | Baseline 25(OH)D, nmol/l[a,g] | VitaminD (IU/d)/ Calcium (mg/d)[d] | Adiposity Measure | Baseline | End of Study[f] | Outcome |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **Jorde et al. (2010)[66] Norway, 3** | D3/ Calcium | 150 | 12 | 46.3 (11.3) | 56 (37.3) | 58.7 (21.2) | 5714/500 | BMI | 34.8 (4.0) | N/A[f] | Lipids and blood pressure |
| | D3/ Calcium | 139 | | 47.3 (11.9) | 50 (35.9) | 56.7 (21.2) | 2857/500 | BMI | 34.4 (3.8) | N/A[f] | |
| | Calcium | 149 | | 48.9 (11.0) | 51 (34.2) | 58.8 (21.0) | −/500 | BMI | 35.1 (3.8) | N/A[f] | |
| **Heikkinen et al. (1997)[67] Finland, 2** | D3/ Calcium | 83 | 36 | 52.8 (0.47) | 0 | N/A | 300/500 | BMI | 26.8 (0.47) | N/A | Lipids |
| | | | | | | | | FM | 71.5 (1.24) | 72.8 (1.38) | |
| | Calcium | 95 | | 52.5 (0.22) | 0 | N/A | −/500 | BMI | 26.4 (0.42) | N/A | |
| | | | | | | | | FM | 67.6 (1.07) | 69.8 (1.26) | |
| **Chandler et al. (2013)[68] USA, 5** | D3/Calcium | 81 | 3 | 51.9 (11.6) | 22 (27.2) | 43.2 (22.3) | 1000/200 | BMI | 32.5 (7.4) | 32.5 (7.4) | Plasma inflammatory markers |
| | | | | | | | | Wt | 89.4 (19.6) | 89.9 (19.9) | |
| | D3/Calcium | 83 | | 51.3 (11.6) | 28 (33.7) | 40.1 (22.1) | 2000/200 | BMI | 33.0 (8.2) | 33.0 (8.2) | |
| | | | | | | | | Wt | 92.7 (23.4) | 92.7 (23.4) | |
| | D3/Calcium | 83 | | 51.5 (11.6) | 29 (34.9) | 44.3 (22.2) | 4000/200 | BMI | 32.2 (7.2) | 32.3 (7.3) | |
| | | | | | | | | Wt | 89.5 (21.5) | 89.9 (21.9) | |
| | Placebo/ Calcium | 81 | | 51.1 (11.1) | 27 (33.3) | 42.5 (23.0) | −/200 | BMI | 31.9 (7.7) | 32.0 (7.9) | |
| | | | | | | | | Wt | 89.6 (20.8) | 90.0 (21.3) | |
| **Aloia et al. (2005)[54] USA, 3** | D3/Calcium | 104 | 36 | 59.9 (6.2) | 0 | 48.1 (20.8) | 800-2000/1200- | BMI | 29 (4.0) | 29.1 (4.8) | Bone mineral density |

| Source/Year/Country /Jadad Score[b] | Treatment Group | Subjects, No. | Duration (months) | Age, years[a] Mean (SD) | Men,n (%) | Baseline 25(OH)D, nmol/l[a,g] | VitaminD (IU/d)/ Calcium (mg/d)[d] | Adiposity Measure | Baseline | End of Study[f] | Outcome |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | 1500 | Wt | 78.0 (13.6) | 76.9 (13.0) | |
| | Calcium | 104 | | 61.2 (6.3) | 0 | 42.9 (16.6) | −/1200-1500 | BMI | 30 (4.0) | 30.6 (4.4) | |
| | | | | | | | | Wt | 79.2 (12.6) | 80.2 (12.6) | |
| **Dawson-Hughes et al. (1991)[59] USA, 3** | D3/Calcium | 124 | 12 | 61.4 (0.5) | 0 | N/A | 400/377 | Wt | 61.4 (0.5) | N/A[f] | Seasonal bone loss |
| | Placebo/ Calcium | 125 | | 61.9 (0.5) | 0 | N/A | −/377 | Wt | 61.9 (0.5) | N/A[f] | |
| **Gallagher et al. (2012)[55] USA, 5** | D3/Calcium | 20 | 12 | 68 (8.6) | 0 | 37.8 (10.8) | 400/ | BMI | 30.3 (5.4) | N/A | Seram 25 (OH)D and PTH |
| | | | | | | | | Wt | 77.8 (13.4) | N/A | |
| | | | | | | | | FM | 31.3 (8.7) | 32.3 (7.1) | |
| | | 21 | | 68 (8.1) | 0 | 39.0 (9.5) | 800/ | BMI | 28.2 (6.1) | N/A | |
| | D3/Calcium | | | | | | | Wt | 74.3 (16.6) | N/A | |
| | | | | | | | | FM | 29.1 (10.7) | 29.9 (12.1) | |
| | | 20 | | 66 (7.4) | 0 | 37.4 (10.2) | 1600/ | BMI | 30.0 (5.4) | N/A | |
| | D3/Calcium | | | | | | | Wt | 76.4 (14.5) | N/A | |
| | | | | | | | | FM | 30.4 (8.8) | 30.8 (9.5) | |
| | | 21 | | 66 (6.3) | 0 | 38.2 (10.1) | 2400/ | BMI | 30.4 (5.4) | N/A | |
| | D3/Calcium | | | | | | | | | | |

| Source/Year/Country /Jadad Score[b] | Treatment Group | Subjects, No. | Duration (months) | Age, years[a] Mean (SD) | Men,n (%) | Baseline 25(OH)D, nmol/l[a,g] | VitaminD (IU/d)/ Calcium (mg/d)[d] | Adiposity Measure | Baseline | End of Study[f] | Outcome |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | Wt | 78.0 (13.0) | N/A | |
| | | | | | | | | FM | 32.0 (8.0) | 33.1 (8.6) | |
| | D3/Calcium | 20 | | 69 (7.7) | 0 | 39.8 (8.2) | 3200/ | BMI | 30.2 (5.7) | N/A | |
| | | | | | | | | Wt | 78.6 (15.8) | N/A | |
| | | | | | | | | FM | 32.2 (9.9) | 32.4 (10.2) | |
| | D3/Calcium | 20 | | 66 (7.1) | 0 | 37.2 (9.2) | 4000/ | BMI | 29.7 (6.4) | N/A | |
| | | | | | | | | Wt | 76.2 (16.2) | N/A | |
| | | | | | | | | FM | 30.1 (10.6) | 31.2 (10.7) | |
| | D3/ Calcium | 20 | | 65 (6.1) | 0 | 38.6 (9.1) | 4800/ | BMI | 32.1 (6.2) | N/A | |
| | | | | | | | | Wt | 83.4 (17.9) | N/A | |
| | | | | | | | | FM | 34.7 (11.1) | 34.6 (10.8) | |
| | Placebo/ Calcium | 21 | | 66 (6.5) | 0 | 37.7 (9.1) | | BMI | 31.1 (5.3) | N/A | |
| | | | | | | | | Wt | 81.3 (16.3) | N/A | |
| | | | | | | | | FM | 33.6 (11.7) | 33.7 (11.6) | |
| **Prince et al. (2008)[60] Australia, 5** | D2/Calci um | 151 | 12 | 77.0 (4.2) | 0 | 45.2 (12.5) | 1000/1000 | BMI | 28.34 (4.92) | 28.37 (4.94) | Risk of falls |
| | | | | | | | | Wt | 71.99 (12.83) | 71.75 (12.79) | |

| Source/Year/Country /Jadad Score[b] | Treatment Group | Subjects, No. | Duration (months) | Age, years[a] Mean (SD) | Men,n (%) | Baseline 25(OH)D, nmol/l[a,g] | VitaminD (IU/d)/ Calcium (mg/d)[d] | Adiposity Measure | Baseline | End of Study[f] | Outcome |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | FM | 28.2 (7.8) | 28.1 (8.1) | |
| | Placebo/ Calcium | 151 | | 77.4 (5.0) | 0 | 44.2 (12.7) | −/1000 | BMI | 29.55 (5.42) | 29.47 (5.45) | |
| | | | | | | | | Wt | 73.94 (14.14) | 73.44 (13.99) | |
| | | | | | | | | FM | 28.1 (8.3) | 30 (8.2) | |
| **Zhu et al. (2008)[50] Australia, 5** | D3/Calcium | 39 | 60 | 75.4 (2.7) | 0 | 70.2 (25.6) | 1000/1200 | BMI | 27.6 (5.1) | 27.8 (5.5) | BMD, biomarkers of bone turnover |
| | | | | | | | | Wt | 67.2 (12.2) | 66.4 (12.7) | |
| | | | | | | | | FM | 24.4 (7.6) | 23.5 (7.6) | |
| | Placebo | 41 | | 74.8 (2.8) | 0 | 67.3 (34.2) | | BMI | 28.0 (6.0) | 28.6 (6.3) | |
| | | | | | | | | Wt | 71.2 (15.2) | 71.5 (15.8) | |
| | | | | | | | | FM | 26.3 (8) | 24.3 (7.5) | |
| | Placebo/ Calcium | 40 | | 74.1 (2.0) | 0 | 66.6 (25.9) | | BMI | 27.9 (6.0) | 28.6 (6.3) | |
| | | | | | | | | Wt | 71.2 (15.2) | 71.5 (15.8) | |
| | | | | | | | | FM | 28.2 (7.7) | 26.2 (7.6) | |
| **Vitamin D and Calcium versus Placebo** | | | | | | | | | | | |
| **Caan et al. (2007)[44] USA, 5** | D3/ Calcium | 18,129 | 84 | 50-79[e] | 0 | N/A | 400/1000 | BMI | 28.9 (6.0) | N/A | Adiposity |
| | | | | | | | | Wt | 76.0 (16.9) | N/A[f] | |
| | Placebo | 18,055 | | 50-79[e] | 0 | N/A | | BMI | 28.8 (6.0) | N/A | |
| | | | | | | | | Wt | 75.9 (17.1) | N/A[f] | |

| Source/Year/Country /Jadad Score[b] | Treatment Group | Subjects, No. | Duration (months) | Age, years[a] Mean (SD) | Men,n (%) | Baseline 25(OH)D, nmol/l[a,g] | VitaminD (IU/d)/ Calcium (mg/d)[d] | Adiposity Measure | Baseline | End of Study[f] | Outcome |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **Major et al. (2007)[69] Canada, 4** | D3/ Calcium | 30 | 3.75 | 43.6 (5.0) | 0 | N/A | 400/1200 | BMI | 31.4 (2.5) | 29.8 (2.8) | Blood pressure, plasma lipid and lipoprotein concentrations, and glucose and insulin concentrations |
| | | | | | | | | Wt | 81.5 (8.3) | 77.5 (9.0) | |
| | Placebo | 33 | | 41.6 (6.1) | 0 | N/A | | BMI | 32.3 (3.5) | 31.1 (3.7) | |
| | | | | | | | | Wt | 83.6 (11.1) | 80.6 (11.7) | |
| **Pittas et al. (2007)[70] USA, 4** | | | | | | | | | | | |
| **NFG** | D3/ Calcium | 108 | 36 | 70.6 (0.4) | 44 (40.7) | 81.4 (3.7) | 700/500 | BMI | 26.1 (0.3) | N/A[f] | insulin sensitivity, plasma C-reactive protein |
| | | | | | | | | Wt | 71.6 (1.2) | N/A | |
| | Placebo | 114 | | 71.7 (0.4) | 41 (35.9) | 70.6 (2.8) | | BMI | 26.2 (0.3) | N/A[f] | |
| **IFG** | D3/ Calcium | 45 | | 71.1 (0.7) | 22 (48.9) | 71.2 (5.2) | 700/500 | Wt | 71.1 (1.2) | N/A | |
| | Placebo | 47 | | 71.3 (0.8) | 26 (55.3) | 81.2 (4.7) | | BMI | 28.1 (0.7) | N/A[f] | |
| | | | | | | | | Wt | 80.0 (2.3) | N/A[f] | |
| **Dawson-Hughes et al. (1997)[56] USA, 3** | | | | | | | | | | | |
| **Men** | D3/ Calcium | 86 | 36 | 70 (4) | 100 | 82.2 (40.6) | 700/500 | Wt | 82.4 (11.3) | N/A[f] | BMD and fractures |
| | Placebo | 90 | | 71 (5) | 100 | 83.7 (31.6) | | Wt | 81.5 (12.8) | N/A[f] | |
| **Women** | D3/ Calcium | 101 | | 71 (4) | 0 | 71.5 (33.1) | 700/500 | Wt | 67.6 (12.1) | N/A[f] | |

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| Source/Year/Country /Jadad Score[b] | Treatment Group | Subjects, No. | Duration (months) | Age, years[a] Mean (SD) | Men,n (%) | Baseline 25(OH)D, nmol/l[a,g] | VitaminD (IU/d)/ Calcium (mg/d)[d] | Adiposity Measure | Baseline | End of Study[f] | Outcome |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | Placebo | 112 | | 72 (5) | 0 | 61.0 (25.7) | | Wt | 68.1 (12.4) | N/A[f] | |

[a] Abbreviations: BMI, body mass index in kg/m$^2$; FM, fat mass; Wt, weight;25 (OH)D, 25-hydroxyvitamin D in nmol/l; FPG, fasting plasma glucose; IFG, impaired fasting glucose; EOS, end of study; N/A: not available; BMD, bone mineral density; SD: standard deviation; IU/d: international units/day; mg/d: milligrams/day;

[b] The 5-point Jadad Score based on the description of randomization, double-blinding, and withdrawals

[c] Ljunghall et al did not report mean (SD) for age;

[d] Ljunghall:Vitamin D ug/day; alphacalcidiol does not have a conversion for IU or an estimation of equivalent dose to vitamin D2 or vitamin D3.

[e] Dawson-Hughes (1991):Mean (SD) of age, 62.4 (6.9), for entire cohort.

[f] Net difference between treatment and placebo group is reported but end of study values are not available

[g] VonHurst: baseline 25 (OH)D is reported as median [quartile 1, quartile 3]

## Table 3

Weighted mean differences of three adiposity measurements by supplementation with vitamin D alone versus placebo or vitamin D plus calcium versus control groups (placebo or calcium)

| Supplement | No. of Studies (treatment/control) | Mean Difference MD (95% CI) | P value for Mean Difference | P value for Heterogeneity Chi-Squared | I squared (%) |
|---|---|---|---|---|---|
| Vitamin D alone vs. placebo | | | | | |
| BMI (kg/m$^2$) | 11 (1123/991) | −0.06 (−0.14, 0.03) | 0.20 | 0.79 | 0 |
| Weight (kg) | 8 (889/766) | −0.05 (−0.32, 0.23) | 0.74 | 0.99 | 0 |
| Fat Mass (kg) | 5 (479/378) | −0.43 (−1.69, 0.84) | 0.51 | <0.001 | 81.2 |
| Vitamin D plus calcium vs. calcium | | | | | |
| BMI (kg/m$^2$) | 7 (1290/978) | 0.02 (−0.11, 0.14) | 0.80 | 0.88 | 0 |
| Weight (kg) | 8 (1380/1073) | 0.12 (−0.24, 0.49) | 0.51 | 0.80 | 0 |
| Fat Mass (kg) | 5 (790/665) | 0.12 (−0.22, 0.45) | 0.50 | 0.42 | 0 |
| Vitamin D alone vs. placebo and vitamin D plus calcium vs. calcium | | | | | |
| BMI (kg/m$^2$) | 18 (2413/1969) | −0.03 (−0.10, 0.04) | 0.36 | 0.92 | 0 |
| Weight (kg) | 16 (2269/1839) | 0.01 (−0.21, 0.23) | 0.90 | 0.99 | 0 |
| Fat Mass (kg) | 10 (1251/1043) | −0.03 (−0.63, 0.57) | 0.92 | <0.001 | 69.9 |
| Vitamin D plus calcium vs. placebo | | | | | |
| BMI (kg/m$^2$) | 6 (744/643) | −0.03 (−0.13, 0.08) | 0.65 | 0.02 | 64 |
| Weight (kg) with WHI* | 5 (18,732/18,623) | −0.13 (−0.21, −0.05) | 0.001 | 0.85 | 0 |
| Weight (kg) without WHI* | 4 (591/482) | −0.19 (−0.88, 0.49) | 0.58 | 0.71 | 0 |
| Fat Mass (kg) | 3 (405/280) | 0.67 (−0.33, 1.66) | 0.19 | 0.83 | 0 |

*Caan et al. (2007)[44], the Women's Health Initiative Vitamin D and Calcium Trial, 36,184 participants, 7 years, 400 IU vitamin D3 plus calcium 1000 mg daily.