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THE ANALYSIS STUDY OF EFFECTIVENESS OF VITAMIN D AND CALCIUM SUPPLEMENTATION FOR PREVENTING OF FRACTURES A COMPREHENSIVE SYSTEMATIC REVIEW

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ABSTRACT

Background: *The interplay between supplementation and other treatments adds complexity to the role of calcium and vitamin D in fracture prevention. This systematic review aims to synthesize existing evidence on the effectiveness of vitamin D and calcium supplementation for fracture prevention based on literatures of the last decade.*

Methods: *The study followed PRISMA 2020 guidelines, reviewing English-language publications from 2014 to 2024. Editorials, duplicate reviews from the same journal, and papers lacking a DOI were excluded. The literature search was conducted using PubMed, SagePub, SpringerLink, and Google Scholar.*

Result: *A total of 2,172 articles were initially identified through online databases (PubMed, SagePub, SpringerLink, and Google Scholar). After three rounds of screening, eight relevant studies were selected for full-text analysis.*

Conclusion: *Vitamin D and calcium supplementation effectively reduce fracture risk, particularly in postmenopausal women and older adults. Adequate intake improves bone mineral density and enhances bone strength, providing significant protection against fractures, especially in those with deficiency.*

Keyword: Vitamin D, calcium, fracture, bone density

INTRODUCTION

Fractures, particularly in older adults, represent a major public health concern, with substantial implications for quality of life and healthcare systems globally. Among the many factors influencing fracture risk, bone health is fundamentally dependent on adequate levels of vitamin D and calcium. These nutrients play pivotal roles in maintaining bone mineral density (BMD), yet their effectiveness as preventative interventions for fractures remains a subject of ongoing debate. [1,2]

Vitamin D plays a critical role in bone health and fracture prevention, as evidenced by research showing significant risks associated with its deficiency. Elderly populations, particularly women, face a markedly higher incidence of hip and osteoporotic fractures when serum 25(OH)D levels remain persistently low. Studies emphasize the protective effects of sufficient vitamin D levels in reducing fracture risk, with some findings suggesting that individuals with optimal levels experience significantly lower fracture rates over long follow-up periods.[3,4]

Calcium, another cornerstone of bone health, has traditionally been associated with strengthening bones and lowering fracture risk. However, emerging evidence has challenged this traditional view by demonstrating limited direct benefits of calcium intake on BMD or bone turnover markers. Research suggests that increasing calcium consumption alone may not significantly reduce fracture rates, particularly in older adults.[5,6]

The interplay between supplementation and other treatments adds complexity to the role of calcium and vitamin D in fracture prevention. Positive associations between calcium intake and BMD observed in studies with high rates of hormone or osteoporosis therapy suggest that the benefits may stem from combined effects rather than calcium supplementation alone.[7,8]

Certain populations may derive specific benefits from supplementation, as illustrated by studies targeting subgroups such as prediabetic males. Evidence indicates that vitamin D3 supplementation helps preserve femoral neck BMD in these individuals, suggesting that targeted interventions could be effective in addressing unique fracture risks. However, the broader applicability of such findings remains uncertain, emphasizing the need for further research into population-specific responses to supplementation to refine preventive strategies.[9,10]

This systematic review aims to synthesize existing evidence on the effectiveness of vitamin D and calcium supplementation for fracture prevention. By analyzing data from diverse studies, the review seeks to clarify the roles of these nutrients in bone health, explore their interaction with other therapeutic measures, and identify effective strategies for reducing fracture risk. Ultimately, the findings aim to contribute to evidence-based practices for improving bone health outcomes across different populations.

METHODS

PROTOCOL

The study strictly adhered to the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) 2020 guidelines to ensure methodological rigor and accuracy. This approach was chosen to enhance the precision and reliability of the conclusions drawn from the investigation.

CRITERIA FOR ELIGIBILITY

This systematic review aims to synthesize existing evidence on the effectiveness of vitamin D and calcium supplementation for fracture prevention based on literatures of the last decade. The review aimed to provide insights to improve patient treatment strategies, with an emphasis on the significance of key findings in the reviewed studies. Inclusion criteria for the study included: 1) Papers published in English, and 2) Papers published between 2014 and 2024. Exclusion criteria were: 1) Editorials, 2) Papers without a DOI, 3) Previously published review articles, and 4) Duplicate entries in journals.

SEARCH STRATEGY

The keywords used for this research are vitamin D, calcium, fracture, bone density. The Boolean MeSH keywords inputted on databases for this research are: *((("vitamin d"[MeSH Terms] OR "vitamin d"[All Fields] OR "ergocalciferols"[MeSH Terms] OR "ergocalciferols"[All Fields]) AND ("calcium"[MeSH Terms] OR "calcium"[All Fields] OR "calciums"[All Fields] OR "calcium s"[All Fields]) AND ("fractur"[All Fields] OR "fractural"[All Fields] OR "fracture s"[All Fields] OR "fractures, bone"[MeSH Terms] OR ("fractures"[All Fields] AND "bone"[All Fields]) OR "bone fractures"[All Fields] OR "fracture"[All Fields] OR "fractured"[All Fields] OR "fractures"[All Fields] OR "fracturing"[All Fields]) AND ("bone density"[MeSH Terms] OR ("bone"[All Fields] AND "density"[All Fields]) OR "bone density"[All Fields])) AND (y_10[Filter]).*

DATA RETRIEVAL

Abstracts and titles were screened to assess their eligibility, and only studies meeting the inclusion criteria were selected for further analysis. Literature that fulfilled all predefined criteria and directly related to the topic was included. Studies that did not meet these criteria were excluded. Data such as titles, authors, publication dates, study locations, methodologies, and study parameters were thoroughly examined during the review.

QUALITY ASSESSMENT AND DATA SYNTHESIS

Each author independently assessed the titles and abstracts of the selected studies to identify those for further exploration. Articles that met the inclusion criteria underwent further evaluation. Final decisions on inclusion were based on the findings from this review process.

Table 1. Article Search Strategy

Database	Keywords	Hits
Pubmed	(("vitamin d"[MeSH Terms] OR "vitamin d"[All Fields] OR "ergocalciferols"[MeSH Terms] OR "ergocalciferols"[All Fields]) AND ("calcium"[MeSH Terms] OR "calcium"[All Fields] OR "calciums"[All Fields] OR "calcium s"[All Fields]) AND ("fractur"[All Fields] OR "fractural"[All Fields] OR "fracture s"[All Fields] OR "fractures, bone"[MeSH Terms] OR ("fractures"[All Fields] AND "bone"[All Fields]) OR "bone fractures"[All Fields] OR "fracture"[All Fields] OR "fractured"[All Fields] OR "fractures"[All Fields] OR "fracturing"[All Fields]) AND ("bone density"[MeSH Terms] OR ("bone"[All Fields] AND "density"[All Fields]) OR "bone density"[All Fields])) AND (y_10[Filter])	466
SpringerLink	(((vitamin D) AND (calcium)) AND (fracture)) AND (bone density)	402
Sagepub	(((vitamin D) AND (calcium)) AND (fracture)) AND (bone density)	500
Google Scholar	(((vitamin D) AND (calcium)) AND (fracture)) AND (bone density)	804

Table 2. JBI *Critical appraisal of Study*

Parameters	Bucheb ner (2014)	Swanso n (2015)	Julian (2016)	Bristo w (2017)	Larsen (2018)	Brist ow (202 2)	Bristo w (2019)	Port hous e (201 5)
1. Bias related to temporal precedence Is it clear in the study what is the "cause" and what is the "effect" (ie, there is no confusion about which variable comes first)?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
2. Bias related to selection and allocation Was there a control group?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
3. Bias related to confounding factors Were participants included in any comparisons similar?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
4. Bias related to administration of intervention/exposure Were the participants included in any comparisons receiving similar treatment/care, other than the exposure or intervention of interest?	No.	No.	No.	No.	No.	No.	No.	No.
5. Bias related to assessment, detection, and measurement of the outcome Were there multiple measurements of the outcome, both pre and post the intervention/exposure?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes

Were the outcomes of participants included in any comparisons measured in the same way?	No.	No.	No.	No.	No.	No.	No.	No.
Were outcomes measured in a reliable way?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
6. Bias related to participant retention								
Was follow-up complete and, if not, were differences between groups in terms of their follow-up adequately described and analyzed?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
7. Statistical conclusion validity								
Was appropriate statistical analysis used?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes

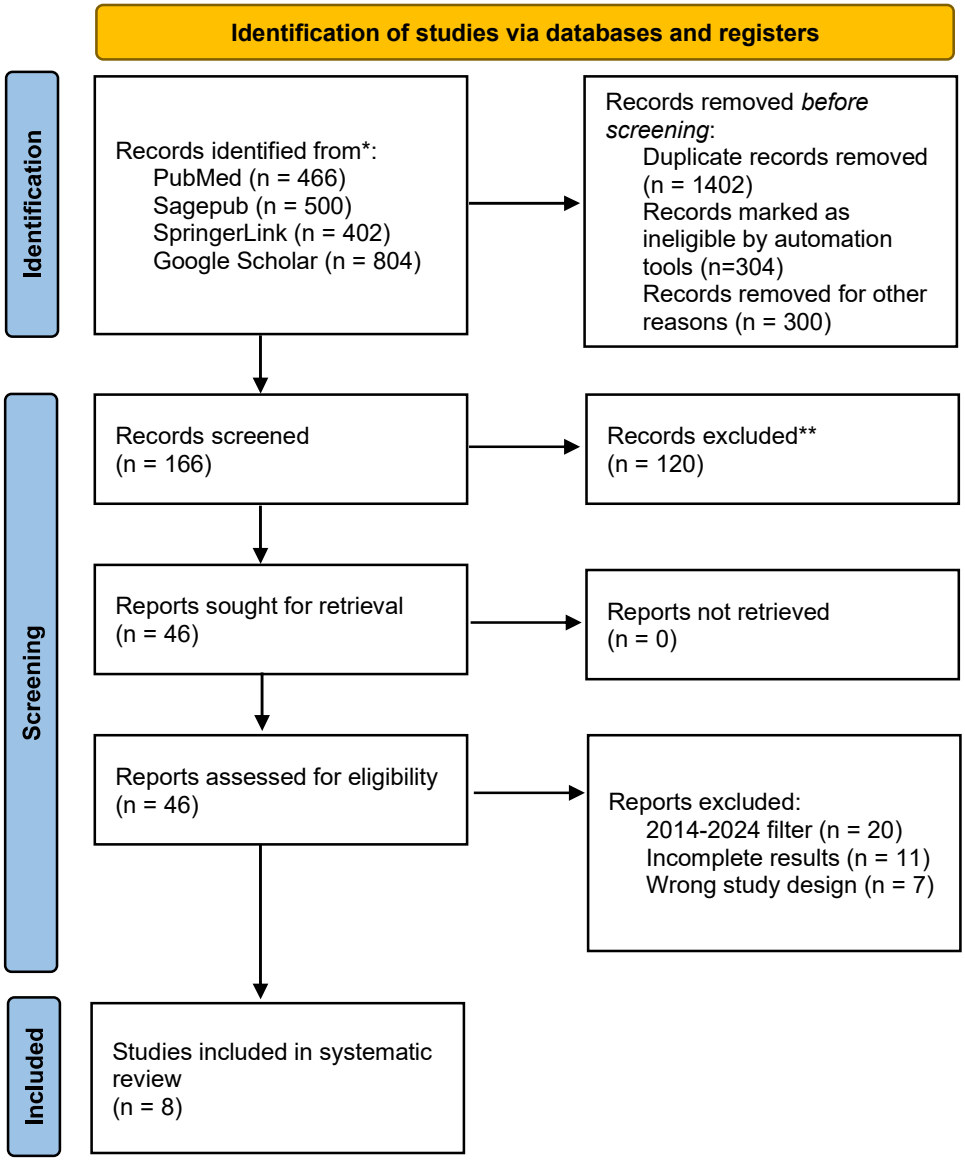

Figure 1. Article search flowchar

RESULT

The initial number of articles retrieved from online databases (PubMed, SagePub, SpringerLink, and Google Scholar) is 2,172 articles. After conducting three levels of screening, eight articles that directly relate to the current systematic review have been chosen for further assessment through full-text reading and analysis. Table 1 presents the selected literature included in this analysis.

Table 1. The literature included in this study

No.	Author	Origin	Method	Sample	Result
1.	Buchebner, et al.[11] (2014)	Sweden	Cohort study	44	Women aged 80–85 with persistently low 25(OH)D levels had a higher hip fracture incidence (22.2% vs. 6.6%; p=0.003) compared to those with high levels. Between ages 80–90, the incidence remained significantly higher in the low category (27.9% vs. 12.3%; p=0.006). Within 5 years, osteoporotic fractures occurred in 50% of the low group versus 34% in the high group (p=0.004), with a 10-year fracture risk notably higher in the low group (HR 2.7 and 1.7; p=0.003 and 0.023).
2.	Swanson, et al.[12] (2015)	USA	Cohort	432	Over an average 5.1-year follow-up, 432 men experienced nonvertebral fractures, including 81 hip fractures. Higher 25(OH)D was linked to greater baseline BMD, slower BMD loss, and lower hip fracture risk, while higher $1,25(OH)_2D$ was associated with lower baseline BMD but not with BMD loss or nonvertebral fracture risk. Men with the lowest $1,25(OH)_2D$ levels (8.70–51.60 pg/mL) had an increased risk of hip fracture (HR 1.99; 95% CI 1.19–3.33), though this association weakened after adjustment for 25(OH)D.
3.	Julian, et al.[13] (2016)	Spain	Cohort	14,624	Fracture incidence was tracked until March 2015. While the age-, sex-, and month-adjusted HRs for fractures across plasma 25(OH)D categories were not significantly different, additional adjustments showed a 29% lower fracture risk for participants with 25(OH)D levels of 50–70 nmol/L compared to those with <30 nmol/L. Physical inactivity at baseline was not associated with fracture risk.
4.	Bristow, et al.[3] (2017)	New Zealand	Retrospective cohort	323	Mean calcium intake was 870 mg/day. Baseline BMD and 2-year bone loss were not associated with calcium intake, even after adjusting for covariables. While calcium intake was inversely correlated with PTH levels ($r = -0.19$, $p = 0.02$), it was not linked to bone turnover markers.
5.	Larsen, et al.[14] (2018)	Norway	Retrospective study	256	A total of 256 participants received vitamin D, and 255 received a placebo, with a baseline mean serum 25(OH)D level of 60 nmol/L. Among completers, males in the vitamin D group experienced significantly less BMD reduction at the femoral neck (0.000 vs. -0.010 g/cm²; p=0.008). No

					significant differences were observed at the total hip site for either sex.
6.	Bristow, et al.[15] (2022)	New Zealand	Retrospective study	23	Most studies (71%) found no association between calcium intake and changes in BMD in men or women. Among women, studies with high rates of hormone or osteoporosis therapy (HT/OT) use (>30%) were more likely to report a positive association (80%) compared to studies with low HT/OT use (10%). No studies in women aged >60 years reported a positive association between calcium intake and BMD changes.
7.	Bristow, et al.[16] (2019)	New Zealand	Observational cohort	1194	The mean calcium intake was 886 mg/day. Baseline BMD and bone loss were not associated with calcium intake across quintiles, regardless of adjustments for age, height, weight, physical activity, alcohol, smoking, or hormone replacement use. Total body bone balance (BMC change) was also unrelated to calcium intake ($p = 0.99$).
8.	Porthouse, et al.[17] (2015)	UK	Retrospective cohort	3314	At 24 months, 69% of women who completed follow-up were still taking supplements. After a median follow-up of 25 months, clinical fracture rates were lower than expected in both groups but showed no significant difference between them (odds ratio for fractures: 1.01, 95% CI 0.71–1.43). The odds ratio for hip fractures was 0.75 (95% CI 0.31–1.78), and fall rates at 6 and 12 months were nearly identical between groups. Quality of life also did not differ significantly.

Buchebner, et al.[11] (2014) showed that persistent 25(OH)D insufficiency over 5 years is linked to increased 10-year risks of hip and major osteoporotic fractures in elderly women.

Swanson, et al.[12] (2015) showed higher 25(OH)D levels are more strongly associated with skeletal outcomes than $1,25(OH)_2D$. The results suggest $1,25(OH)_2D$ offers limited additional predictive value for adverse skeletal outcomes when 25(OH)D is measured.

Julian, et al.[13] (2016)showed that vitamin D status was inversely related to fracture risk in middle-aged adults, with a J-shaped relationship observed in older adults. Findings may reflect the influence of vitamin D supplementation practices, though long follow-up and potential exposure changes limit definitive conclusions.

Bristow, et al.[3] (2017) showed that calcium intake had no significant effect on BMD or bone loss in men, suggesting that increasing calcium intake is unlikely to reduce the prevalence or morbidity of male osteoporosis.

Larsen, et al.[14] (2018) concludes that Vitamin D3 supplementation may help preserve femoral neck BMD in males with prediabetes, but further studies are required to confirm this effect.

Bristow, et al.[15] (2022) showed that Calcium intake (typically >500 mg/day) is not a significant determinant of bone loss, especially in women over 60. Positive findings in some studies may be confounded by co-administration of calcium with HT/OT treatments.

Bristow, et al.[16] (2019) concluded that Postmenopausal bone loss is not influenced by dietary calcium intake, indicating that increasing calcium intake is unlikely to affect the prevalence or severity of postmenopausal osteoporosis.

Porthouse, et al.[17] (2015) showed that Calcium and vitamin D supplementation does not reduce the risk of clinical fractures in women with risk factors for hip fracture.

DISCUSSION

Vitamin D and calcium play critical roles in bone health, yet their effectiveness in preventing fractures varies depending on individual factors, such as age, baseline nutritional status, and co-existing medical conditions. Persistent vitamin D deficiency, as demonstrated by Buchebner et al. (2014), substantially increases the risk of hip and osteoporotic fractures in elderly women. This study highlighted a nearly threefold increase in 10-year fracture risk among women with low serum 25(OH)D levels compared to those with adequate levels, emphasizing the necessity of maintaining optimal vitamin D status for skeletal health.[11]

The relationship between vitamin D status and fracture risk underscores its critical role in maintaining bone integrity. Julian et al. (2016) found that adequate vitamin D levels inversely correlated with fracture risk in middle-aged adults, although a J-shaped relationship was observed in older adults.[13] Similarly, Swanson et al. (2015) demonstrated that higher 25(OH)D levels were linked to improved baseline bone mineral density (BMD) and reduced hip fracture risk. However, their study also highlighted the limited predictive value of $1,25(OH)_2D$ for fracture outcomes, suggesting that serum 25(OH)D should remain the primary biomarker in assessing vitamin D-related skeletal health.[12]

Calcium intake alone appears to have a limited role in fracture prevention and bone health, as shown in several studies. Bristow et al. (2017, 2019) found no significant associations between dietary calcium intake and changes in BMD or bone turnover markers in both men and postmenopausal women. These findings indicate that increasing calcium intake beyond a certain threshold is unlikely to impact the prevalence or morbidity of osteoporosis significantly, particularly in older populations.[3,16]

The interplay of calcium supplementation with other therapies may influence its observed effects on bone health. Bristow et al. (2022) reported that studies with high rates of co-administration of calcium and hormone or osteoporosis therapies (HT/OT) were more likely to find positive associations between calcium intake and BMD changes. This suggests that the apparent benefits of calcium may be confounded by the effects of concurrent therapeutic interventions, underscoring the need for careful interpretation of study outcomes.[15]

The combination of vitamin D and calcium supplementation has shown limited effectiveness in preventing fractures in general populations. Porthouse et al. (2015) observed no significant differences in clinical fracture rates, fall incidence, or quality of life between groups receiving combined supplementation and those on placebo, even among women with elevated hip fracture risk. These findings challenge the widespread use of combined supplementation as a universal preventive strategy against fractures.[17]

Certain populations may derive specific benefits from targeted vitamin D supplementation. Larsen et al. (2018) found that males with prediabetes who received vitamin D3 supplementation experienced significantly less BMD reduction at the femoral neck, a finding not observed at other skeletal sites. This suggests that vitamin D supplementation may have site-specific benefits in particular subgroups, though additional research is required to confirm these effects and understand their clinical implications.[14]

Optimal dosages of vitamin D and calcium are essential for effective fracture prevention, with evidence pointing to the importance of maintaining serum 25(OH)D levels between 50–70 nmol/L to reduce fracture risk. Levels below 30 nmol/L, as seen in Buchebner et al. (2014) and Julian et al. (2016), were consistently associated with higher fracture risks.[11,13] For calcium, daily intakes exceeding 500 mg appear to provide no additional benefit for bone health, especially in older populations, according to findings by Bristow et al. (2022).[15]

The limitations inherent in existing studies complicate the interpretation of findings and their application to broader populations. Variability in baseline characteristics, long follow-up periods, and changes in exposure over time contribute to heterogeneity in results. Additionally, confounding by concurrent therapies, as noted by Swanson et al. (2015) and Porthouse et al. (2015), complicates efforts to attribute observed outcomes solely to vitamin D or calcium supplementation.[12,17]

Given the mixed evidence, public health strategies should prioritize addressing deficiencies in high-risk groups rather than advocating universal supplementation. Elderly individuals, particularly those with prediabetes or persistently low vitamin D levels, may benefit from targeted interventions tailored to their specific needs. At the same time, caution should be exercised to avoid excessive supplementation, which could lead to potential adverse effects. Future research should aim to refine supplementation guidelines through large-scale, randomized controlled trials that account for individual variability

and therapy interactions. A personalized approach that considers specific risk factors and baseline nutritional status may prove more effective in preventing fractures and optimizing bone health across diverse populations.[18]

CONCLUSION

Vitamin D and calcium supplementation effectively reduce fracture risk, particularly in postmenopausal women and older adults. Adequate intake improves bone mineral density and enhances bone strength, providing significant protection against fractures, especially in those with deficiency.

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