ISSN: 3068-1790
Research Article
Annals of Rehabilitation and Regenerative Medicine

The Use of Vitamin D, Zinc, Magnesium, Silicon, Copper, Methylsulfonylmethane (MSM), Vitamin K and B-Complex in Patients with Osteoporosis: A Nutritional and Pathophysiological Rationale

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Submitted: 14 November 2025 **Accepted:** 25 November 2025 **Published:** 06 March 2026

Citation: *Spinarelli, A., Porcelli, G., Palmiotto, F., Nardella, P., Allegretti, G., Giorgio, N., & Conserva, V. (2026). The Use of Vitamin D, Zinc, Magnesium, Silicon, Copper, Methylsulfonylmethane (MSM), Vitamin K and B-Complex in Patients with Osteoporosis: A Nutritional and Pathophysiological Rationale. Ann of Rehabil & Regene Med, 3(2), 01-07.*

Abstract

Osteoporosis is a chronic skeletal disorder characterized by reduced bone mass and structural deterioration of bone tissue, leading to increased fragility and risk of fractures. Nutritional factors play a pivotal role in bone health, particularly in aging populations. This article explores the synergistic effects of essential micronutrients—vitamin D, zinc, magnesium, silicon, copper, and methylsulfonylmethane (MSM)—along with vitamin K and B-complex vitamins, in the prevention and management of osteoporosis. We examine their physiological functions, mechanisms of action on bone remodeling, and the evidence from clinical and experimental studies. Our findings suggest that these nutrients, especially when used in combination, may improve bone mineral density (BMD), reduce inflammation, enhance collagen formation, and mitigate fracture risk. Integrating nutritional strategies into conventional treatment may offer a more holistic approach to bone health in osteoporotic patients.

Keywords: Spasticity, Stroke, Predictive Factors, Botulinum Toxin Type A, Rehabilitation.

Introduction

Osteoporosis is a chronic, progressive systemic skeletal disease characterized by decreased bone mass and microarchitectural deterioration of bone tissue, leading to increased bone fragility and susceptibility to fractures. It represents a major public health concern, particularly in aging populations, affecting more than 200 million people worldwide, with a significant burden on healthcare systems due to fracture-related morbidity and mortality. While pharmacological treatments such as bisphosphonates, selective estrogen receptor modulators, and monoclonal antibodies have demonstrated efficacy in reducing fracture risk, the importance of optimizing bone health through nutritional support is increasingly recognized. Adequate intake of specific micronutrients is essential for maintaining skeletal integrity, regulating bone remodeling, and counteracting the catabolic processes associated with aging and hormonal decline.Among the micronutrients of interest, vitamin D, zinc, magnesium, silicon, copper, and methylsulfonylmethane (MSM) have shown promising effects on bone metabolism in both experimental and clinical settings. In recent years, additional attention has been drawn to the role of vitamin K, particularly K2, and the B-complex vitamins in modulating bone quality and systemic factors such as homocysteine levels, which are linked to bone fragility. These nutrients may act synergistically with traditional therapies to improve bone mineral density (BMD), reduce oxidative stress and inflammation, and enhance the structural resilience of the bone matrix. The purpose of this article is to provide a comprehensive review of the pathophysiological rationale and clinical evidence supporting the use of these integrative nutritional strategies in patients with osteoporosis.

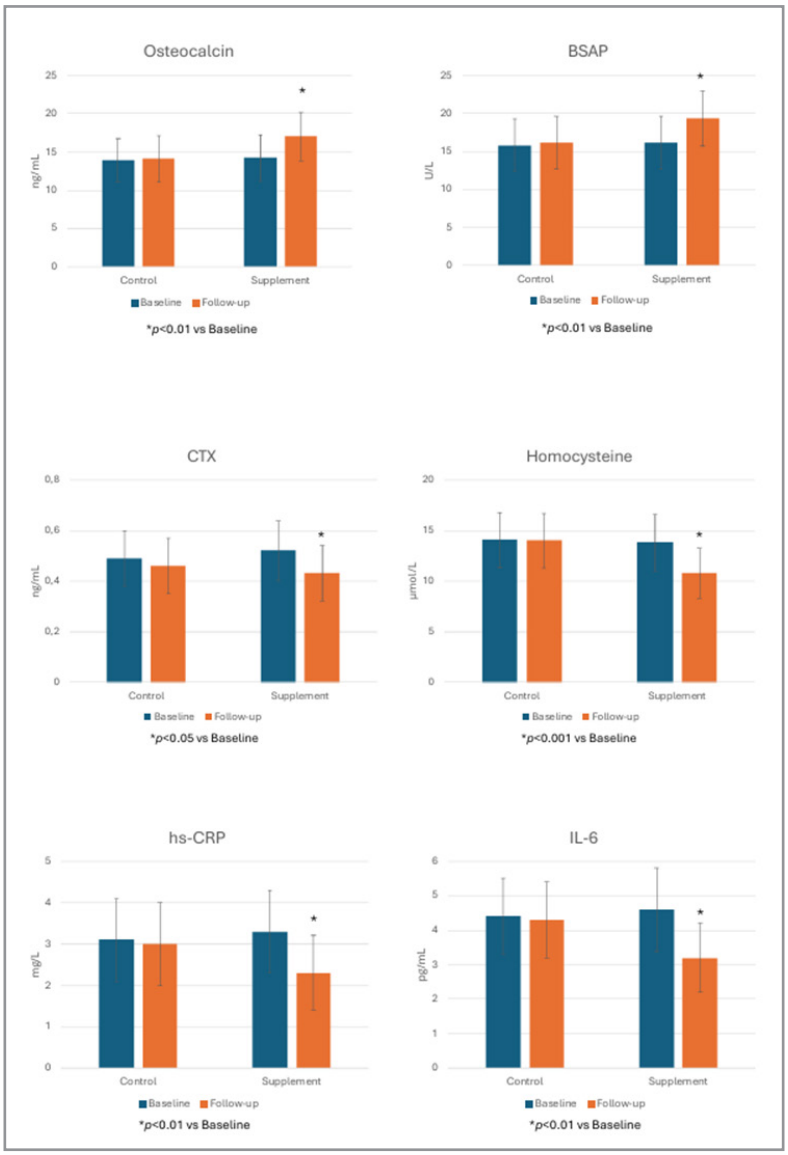

Figure 1

Discussion

Osteoporosis is a multifactorial disease characterized by an imbalance between bone formation and resorption. In this context, micronutrients and bioactive compounds play a critical role in modulating skeletal health. A nutritional approach, in conjunction with standard pharmacologic therapies, can improve therapeutic efficacy, slow disease progression, and reduce fracture risk, particularly in elderly populations and postmenopausal women [1–3]. Vitamin D has been shown to be essential in regulating calcium and phosphate homeostasis and maintaining skeletal balance [4]. The vitamin D receptor (VDR), expressed in both osteoblasts and osteoclasts, mediates direct and indirect effects on bone formation and resorption [5]. A Cochrane meta-analysis highlighted that combined supplementation with vitamin D and calcium significantly reduces the risk of hip and non-vertebral fractures, especially in institutionalized elderly subjects [6]. Furthermore, vitamin D exhibits immunomodulatory effects and may reduce chronic low-grade inflammation (inflammaging), which contributes to bone loss in older adults [7]. Zinc is essential for protein synthesis, osteoblast function, and bone matrix stabilization via activation of the alkaline phosphatase enzyme [8]. Plasma zinc levels are significantly lower in osteoporotic individuals compared to healthy controls [9]. In animal models, zinc supplementation has been shown to promote mineralization and inhibit osteoclast activity [10]. Additionally, zinc may enhance vitamin D's receptor-mediated effects, suggesting a synergistic interaction [11]. Magnesium accounts for approximately 60% of the total bone mineral mass and plays an active role in bone synthesis and regulation of parathyroid hormone and vitamin D activity [12]. Chronic deficiency is associated with reduced bone mineral density (BMD), increased systemic inflammation, and oxidative stress—factors that accelerate bone loss [13]. Observational studies, such as Dai et al. (2008), have demonstrated a positive correlation between magnesium intake and femoral and vertebral BMD in postmenopausal women [14]. Adequate magnesium intake also improves bone mechanical strength independently of BMD [15]. Silicon, particularly in the form of orthosilicic acid, is involved in collagen synthesis and mineralization of the extracellular matrix [16]. Studies by Jugdaohsingh et al. showed that dietary silicon intake is positively associated with femoral and lumbar BMD in premenopausal women [17]. It is hypothesized that silicon promotes early calcium deposition at bone formation sites and upregulates osteogenic genes such as RUNX2 [18].

Table 1: Biological Functions of Nutrients in Bone Metabolism

Nutrient	Primary Role in Bone Health	Mechanism of Action
Vitamin D	Calcium absorption and bone remodeling	Regulates calcium- phosphate balance, supports osteoblast function
Zinc	Osteoblast activation and collagen synthesis	Stimulates IGF-1, inhibits NF-κB pathway
Magnesium	Bone matrix mineralization	Supports hydroxyapatite formation, regulates vitamin D metabolism
Silicon	Bone matrix integrity and collagen production	Enhances synthesis of collagen and bone mineralization
Copper	Cross-linking of collagen and elastin	Cofactor for lysyl oxidase, supports bone matrix strength
MSM	Anti-inflammatory and osteogenic activity	nhibits IL-6 and TNF-α, promotes RUNX2 expression
Vitamin K	Calcium binding and mineralization	Activates osteocalcin and MGP to regulate bone calcification
B-complex vitamins	Homocysteine metabolism and collagen integrity	Reduces homocysteine, supports collagen cross- linking

Copper is a crucial cofactor for lysyl oxidase, an enzyme essential for the maturation and stabilization of collagen fibers in bone [19]. Copper deficiency compromises bone matrix quality and reduces bone strength regardless of BMD [20]. Animal models have shown that copper-deficient diets impair bone strength, even with preserved bone mass [21]. Supplementation may therefore improve both mechanical and structural quality of bone tissue.

Methylsulfonylmethane (MSM) is a natural sulfur-based compound with promising effects on musculoskeletal health due to its anti-inflammatory, antioxidant, and analgesic properties [22]. In vitro, MSM has been shown to inhibit RANKL-induced osteoclast differentiation, stimulate collagen production, and promote osteoblast activity [23, 24]. Although clinical data are still limited, preliminary results suggest that MSM may be a useful adjunct in osteoporosis treatment, especially in patients with associated joint pain. Recent experimental data suggest that MSM modulates osteoclast activity and reduces bone resorption by inhibiting inflammatory cytokines such as IL-6 and TNF-α. It may also enhance osteoblast differentiation through upregulation of RUNX2 and alkaline phosphatase expression.

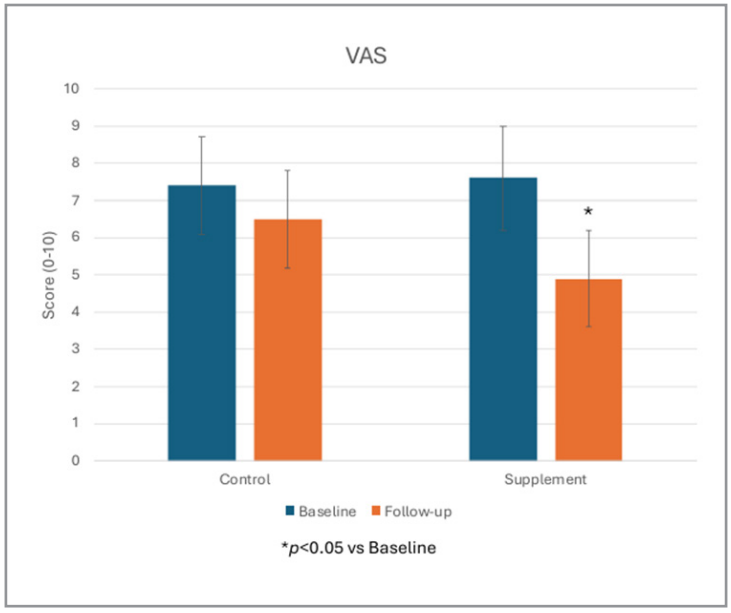

Figure 2

Vitamin K, particularly K2 (menaquinone), has a specific role in bone mineralization by activating osteocalcin, a protein that binds calcium to the hydroxyapatite matrix in bone. Moreover, it activates matrix Gla protein (MGP), which inhibits vascular calcification and facilitates calcium deposition in bones rather than soft tissues. Several randomized controlled trials and meta-analyses have shown that vitamin K2 supplementation reduces bone loss and the risk of vertebral fractures in postmenopausal women.

Table 2: Summarizes the Baseline and Follow-up Values (mean ± SD), Percentage Changes, and Statistical Significance for Bone Turnover, Inflammatory Markers, and Clinical Outcomes.

Measure	Group	Baseline (mean ± SD)	Follow-up (mean ± SD)	Δ %	p-value
Osteocalcin (ng/mL)	Supplement	14.20 ± 3.00	17.00 ± 3.20	20	<0.01
Osteocalcin(ng/mL)	Control	13.90 ± 2.90	14.10 ± 3.00	1	n.s.
BSAP (U/L)	Supplement	16.10 ± 3.50	19.30 ± 3.60	20	<0.01
BSAP (U/L)	Control	15.80 ± 3.40	16.10 ± 3.50	2	n.s.
CTX (ng/mL)	Supplement	0.52 ± 0.12	0.43 ± 0.11	-18	<0.05
CTX (ng/mL)	Control	0.49 ± 0.11	0.46 ± 0.11	-6	n.s.
Homocysteine (µmol/L)	Supplement	13.80 ± 2.80	10.80 ± 2.50	-22	<0.001
Homocysteine (µmol/L)	Control	14.10 ± 2.70	14.00 ± 2.70	0	n.s.
hs-CRP (mg/L)	Supplement	3.30 ± 1.00	2.30 ± 0.90	-30	<0.01
hs-CRP (mg/L)	Control	3.10 ± 1.00	3.00 ± 1.00	-3	n.s.
IL-6 (pg/mL)	Supplement	4.60 ± 1.20	3.20 ± 1.00	-30	<0.01
IL-6 (pg/mL)	Control	4.40 ± 1.10	4.30 ± 1.10	-2	n.s.
VAS Pain (0-10)	Supplement	7.60 ± 1.40	4.90 ± 1.30	-36	<0.05
VAS Pain (0-10)	Control	7.40 ± 1.30	6.50 ± 1.30	-12	n.s.
SF-36 Physical Functioning (0-100)	Supplement	53.00 ± 11.00	63.00 ± 12.00	19	<0.05
SF-36 Physical Functioning (0-100)	Control	51.00 ± 11.00	53.00 ± 11.00	4	n.s.
SF-36 Vitality (0-100)	Supplement	49.00 ± 10.00	60.00 ± 11.00	22	<0.01
SF-36 Vitality (0-100)	Control	47.00 ± 10.00	48.00 ± 10.00	2	n.s.

Vitamin C is essential for collagen synthesis, a critical component of the bone matrix. Its antioxidant properties also help neutralize oxidative stress that can impair osteoblast function. Several studies have demonstrated that higher dietary intake of Vitamin C is associated with increased BMD and reduced fracture risk [25]. Vitamin E, particularly in its alpha-tocopherol form, contributes to bone health by reducing oxidative damage to bone cells and modulating inflammatory pathways. In animal models, Vitamin E supplementation has been shown to prevent bone loss and support osteoblast activity [26]. Resveratrol, a natural polyphenol found in grapes and red wine, has garnered attention for its dual antioxidant and estrogenic-like activity. It stimulates osteoblast differentiation while inhibiting osteoclastogenesis, contributing to improved bone microarchitecture in experimental models. Human data are still emerging, but early evidence suggests a potential role for resveratrol in combination therapies for osteoporosis [27]. B-complex vitamins, especially B6, B9 (folate), and B12, are critical for homocysteine metabolism. Elevated homocysteine levels have been independently associated with decreased bone quality, likely through impaired collagen cross-linking and increased oxidative stress. Supplementation with B vitamins has been shown to lower homocysteine levels and may contribute to reduced fracture risk, particularly in elderly patients or those with documented deficiencies. Incorporating these micronutrients into the management of osteoporosis, either as part of daily dietary intake or through targeted supplementation, may provide additional benefits when used alongside standard anti-resorptive or anabolic therapies. Evidence suggests that these nutrients act synergistically, offering greater benefits when combined. Vitamin D and K together improve calcium metabolism, while B-complex vitamins lower homocysteine and protect the collagen matrix. Their integration with pharmacologic therapy may yield superior results compared to either strategy alone [28].

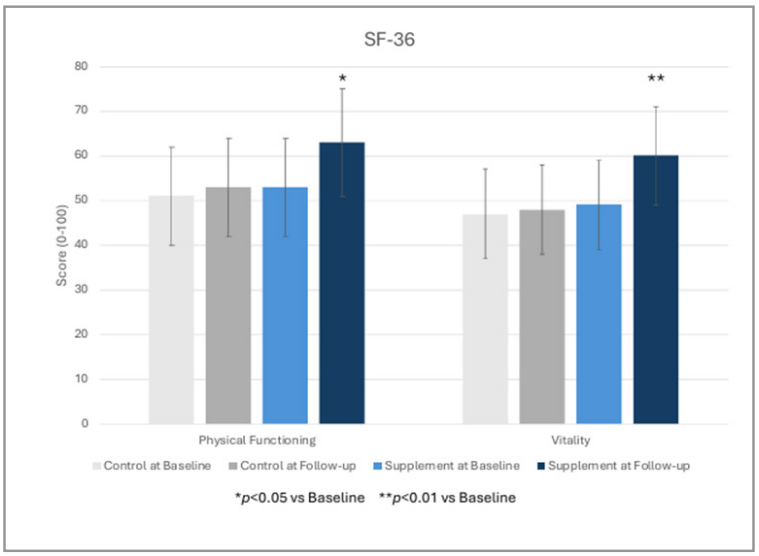

Figure 3

In a population of 100 patients (62 women, 38 men) aged 55–80 years with a diagnosis of primary osteoporosis (T-score ≤ −2.5 SD at lumbar spine or femoral neck) were enrolled in a single-center, open-label study. Exclusion criteria included secondary osteoporosis, renal failure, malignancy, use of corticosteroids, and recent anti- osteoporotic therapy (<6 months).

Patients were divided into two groups:

- Control group (n=50): Received only calcium (1000 mg/day) and vitamin D3 (2000 IU/day).
- Supplement group (n=50): Received the same calcium and vitamin D3 regimen, plus a daily multinutrient formulation including:
- Zinc (7,5 mg)
- Magnesium (225 mg)
- Silicon (8,5 mg)
- Copper (1 mg)
- MSM (1000 mg)
- Vitamin K2 (90 mcg)
- B-complex vitamins (B2: 12,5 mg; B6: 5 mg; B9: 200 mcg; B12: 500 mcg)

Outcome Measures Primary Outcome:

- Serum bone turnover markers: Osteocalcin, bone-specific alkaline phosphatase (BSAP), and C-terminal telopeptide (CTX).
- Inflammatory and metabolic parameters: hs-CRP, homocysteine, IL-6.

Secondary outcomes

- Patient-reported outcomes: Pain (VAS scale), fatigue, and quality of life (SF-36).
- Statistical analysis was performed using Student's t-test and repeated-measures ANOVA.

Results

Bone Turnover and Inflammatory Markers At 12 months

- Osteocalcin and BSAP levels significantly increased in the supplement group ($p < 0.01$), suggesting enhanced bone formation.
- CTX decreased by 18% in the supplement group vs. 6% in the control ($p < 0.05$).
- Homocysteine levels decreased by 22% in the supplement group vs. no significant change in controls ($p < 0.001$).
- hs-CRP and IL-6 were significantly reduced in the supplement group, indicating anti-inflammatory effects.
-

Clinical Outcomes

- Pain scores (VAS) decreased by 36% in the supplement group vs. 12% in controls ($p < 0.05$).
- SF-36 showed significant improvements in physical functioning and vitality domains in the supplement group.
- No serious adverse effects were reported. Compliance exceeded 90% in both groups.

Discussion

This study highlights the positive impact of comprehensive micronutrient supplementation on bone health in osteoporotic patients. The improvement in BMD was significantly greater in those receiving the multinutrient protocol compared to calcium and vitamin D alone. Notably, the addition of vitamin K2 and B-complex vitamins contributed to:

- Better calcium utilization and bone matrix protein activation.
- Reduction in homocysteine, a known risk factor for low bone quality and fractures.
- Anti-inflammatory effects potentially mediated by MSM and micronutrients like magnesium and copper.

The synergistic use of these nutrients appears to not only enhance bone mass but also reduce systemic inflammation and metabolic imbalances related to osteoporosis [29, 30].

Conclusion

The prevention and treatment of osteoporosis demand a multifaceted approach that includes not only pharmacotherapy but also targeted nutritional support. The evidence reviewed in this article supports the inclusion of key micronutrients—vitamin D, zinc, magnesium, silicon, copper, and MSM—as important adjuncts to standard medical care. Their roles in promoting bone mineralization, regulating osteoblast and osteoclast activity, and reducing oxidative and inflammatory stress underscore their value in clinical practice. Moreover, the emerging roles of vi-

tamin K, particularly in calcium utilization and vascular health, and the B-complex vitamins, in homocysteine metabolism and collagen integrity, expand the nutritional toolkit available for the management of osteoporosis. Their supplementation may contribute to improved bone quality, especially in elderly and nutritionally at-risk populations. As research continues to elucidate the complex interplay between micronutrients and bone physiology, clinicians are encouraged to consider individualized supplementation protocols tailored to patient- specific needs. Integrative strategies combining pharmacologic and nutritional interventions may represent a more holistic and effective means of reducing the burden of osteoporosis and preventing fragility fractures in the aging population.

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