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ISSN: 2836-2276 Open Access

Journal of Food and Nutrition

Editorial Letter

Muscle & Bone Health After 40

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Received Date: 04 June 2026; **Accepted Date:** 29 July 2026; **Published Date:** 11 August 2026

Abstract

Osteosarcopenia is now recognised as one of the most clinically significant musculoskeletal conditions of ageing. Both sarcopenia and osteoporosis share common pathophysiological roots: declining levels of anabolic hormones (including oestrogen,-testosterone and insulin-like growth factor-1), rising systemic inflammation driven by pro-inflammatory cytokines such as interleukin-6 and tumour necrosis factor-alpha, impaired mitochondrial function, and deteriorating nutritional status. When muscle mass declines, the mechanical stimulation of bone is reduced, accelerating bone loss and conversely, reduced bone quality impairs the structural framework that supports muscular attachment and function. This interplay means that addressing bone and muscle health in isolation is scientifically inadequate; they must be approached as a unified biological system. The five main pathological processes driving bone and muscle loss after 40 are: (1) declining anabolic hormone signaling [addressed by boron and zinc]; (2) rising inflammatory cytokines [addressed by vitamin D, C, and magnesium]; (3) declining collagen synthesis [addressed by ch-OSA and vitamin C]; (4) impaired calcium regulation [addressed by vitamin D, K2, and magnesium]; (5) elevated homocysteine [addressed by B12 and B1]. This formulation addresses all five pathways.

Keywords: Osteosarcopenia, Pathophysiological roots, Interleukin-6 and Tumour necrosis factor-alpha, Vitamin D, C, and magnesium.

Understanding Osteosarcopenia

Osteosarcopenia is an emerging clinical syndrome defined by the simultaneous presence of sarcopenia — the progressive, age-related loss of skeletal muscle mass, strength, and physical function — and osteopenia or osteoporosis, characterised by reduced bone mineral density and deterioration of bone microarchitecture. First formally described as a unified entity in the early 2010s, osteosarcopenia is now recognised as one of the most clinically significant musculoskeletal conditions of ageing. Both sarcopenia and osteoporosis share common pathophysiological roots: declining levels of anabolic hormones (including oestrogen, testosterone and insulin-like growth factor-1), rising systemic inflammation driven by pro-inflammatory cytokines such as interleukin-6 and tumour necrosis factor-alpha, impaired mitochondrial function, and deteriorating nutritional status. The two conditions also share a bidirectional biological relationship: muscle tissue exerts direct mechanical forces on bone through contraction, stimulating bone remodelling and maintaining density, while bone-derived hormones such as osteocalcin act back on muscle to regulate glucose uptake and contractile function. When muscle mass declines, the mechanical stimulation of bone is reduced, accelerating bone loss and conversely, reduced bone quality impairs the structural framework that supports muscular attachment and function. This interplay means that addressing bone and muscle health in isolation is scientifically inadequate; they must be approached as a unified biological system.

The prevalence of osteosarcopenia rises sharply with age

and represents a major public health burden. Estimates suggest that osteosarcopenia affects between 5% and 37% of community-dwelling older adults depending on the population studied and the diagnostic criteria applied, with rates considerably higher in residential care settings. Individuals with osteosarcopenia face substantially greater risks than those with either condition alone: meta-analyses have demonstrated a two- to fourfold increase in fall risk, a three- to fivefold increase in fracture risk, greater rates of functional decline and disability, higher all-cause mortality, and significantly worse health-related quality of life compared to age-matched peers without the syndrome. Critically, the biological changes that drive osteosarcopenia begin long before clinical thresholds are crossed muscle mass and bone density both begin declining from the third and fourth decades of life, with the rate of loss accelerating markedly after 50, and more rapidly again in women following menopause. This makes the fourth decade — the over-40 window — the most important and actionable time for preventive nutritional and lifestyle intervention. Targeted nutritional support addressing the shared molecular drivers of both bone and muscle decline has been identified in systematic reviews and international guidelines as a cornerstone of osteosarcopenia prevention, alongside resistance exercise. The nine-component formulation described in this document was designed specifically to address these shared pathways, with each ingredient selected on the basis of its evidence-based contribution to either bone mineralisation, muscle anabolism, collagen integrity, anti-inflammatory action, or hormonal and metabolic regulation — and in many cases, more than one of these simultaneously.

Osteosarcopenia: epidemiology, diagnosis, and treatment — facts and numbers. J Cachexia Sarcopenia Muscle, 11(3):609-618. Estimated prevalence 5-37% in community-dwelling older adults; osteosarcopenia associated with 3-5x higher fracture risk and significantly increased mortality compared to either condition alone. Also: [1-2] Beyond Calcium and Vitamin D in Osteosarcopenia. Nutrients, PMC12300471. Also: [3] Nutritional Supplementation for Better Muscle Health in Older Adults. OBM Geriatrics, 9(1):296 — confirmed nutritional interventions targeting shared bone-muscle pathways are a cornerstone of osteosarcopenia prevention alongside resistance exercise.

15-Point Evidence Summary

01. Vitamin D 2,000 IU activates the genetic machinery for muscle protein synthesis and bone mineralisation

Vitamin D acts directly on skeletal muscle cells via vitamin D receptors (VDRs), regulating genes involved in muscle protein synthesis, calcium handling, and neuromuscular coordination. At 2,000 IU daily — well within the safe ceiling of 4,000 IU — this formulation provides a clinically meaningful dose sufficient to correct the widespread deficiency prevalent in adults over 40.

Evidence: Associations Between Vitamin D Deficiency and Sarcopenia in South Korean Adults. Nutrients, 17(20):3292. Among 3,920 participants, men with vitamin D deficiency had significantly higher odds of low muscle mass (OR 1.82; 95% CI 1.10-3.02) and sarcopenia (OR 2.30; 95% CI 1.03-5.16) compared to those without deficiency, after adjusting for age, BMI, and energy intake.[4]

02. Magnesium Bisglycinate 140 mg unlocks vitamin D, supports muscle contraction, and is the best-tolerated form for daily use

Magnesium is required for two critical enzymatic steps that convert inactive vitamin D into its biologically active form, 1,25-dihydroxyvitamin D — without it, even high-dose vitamin D supplementation cannot be properly activated. Approximately 60% of the body's magnesium is stored in bone, and it is directly required for calcium ion transport across cell membranes — the key trigger for every muscle contraction. This formulation uses magnesium bisglycinate specifically: a chelated form in which magnesium is bound to two glycine molecules, resulting in significantly higher bioavailability and near-elimination of the laxative and gastrointestinal side effects (loose stools, cramping) that affect many users of cheaper forms such as magnesium oxide or citrate. At 140 mg of elemental magnesium, this dose delivers a clinically meaningful amount of highly bioavailable magnesium well within the safe supplemental upper limit of 350 mg/day.
Magnesium status and supplementation influence vitamin D status and metabolism: results from a randomised trial. Am J Clin Nutr, 112(3):750-759.[5] Also: [6] Bioavailability of magnesium diglycinate versus magnesium oxide in patients with ileal resection. J Parenter Enteral Nutr, 18(5):430-435 — demonstrated significantly higher absorption of glycinate-chelated magnesium. Mg citrate found more bioavailable than other Mg preparations in a randomised, double-blind study. Magnes Res, 16(3):183-191. [6-b]. Magnesium bisglycinate as safe form for mineral supplementation in human nutrition. OM & Ernahrung, 144:1-16 — confirmed bisglycinate as the superior-tolerated form with minimal GI side effects compared to inorganic salts. Schwalfenberg [6-c]. The Importance of Magnesium in Clinical Healthcare. Scientifica — confirmed magnesium as a mandatory cofactor for vitamin D activation and muscle membrane calcium transport.

03. Vitamin K2 100 mcg directs calcium into bone and away from arteries

Vitamin K2 (MK-7) activates two key proteins: osteocalcin, which embeds calcium into bone matrix, and matrix Gla pro-

tein (MGP), which prevents calcium from depositing in arteries and soft tissues. This makes K2 the essential 'traffic director' for the calcium absorbed via vitamin D — without it, increased calcium absorption may raise cardiovascular calcification risk rather than bone density.

Evidence: Effects of vitamin K supplementation on bone mineral density at different sites and bone metabolism in middle-aged and elderly population: a meta-analysis and systematic review of 17 RCTs including 4,800 subjects. Bone Joint Res, 13(12):750-763. Concluded that vitamin K supplementation enhances carboxylation of osteocalcin, supporting bone formation markers.[7] Also: [8] The Synergistic Interplay between Vitamins D and K for Bone and Cardiovascular Health. Int J Endocrinol, 2017:7454376.

04. The Vitamin D + K2 + Magnesium triad works synergistically — each amplifies the others

These three nutrients form the most evidence-supported triad in musculoskeletal supplementation. Vitamin D stimulates intestinal calcium absorption; K2 ensures absorbed calcium is directed to bones rather than arteries; and magnesium is essential for vitamin D activation and calcium transport. When taken together, each ingredient enhances the effectiveness of the others in ways none achieves in isolation.

Evidence: Growing Evidence of a Proven Mechanism Shows Vitamin K2 Can Impact Health Conditions Beyond Bone and Cardiovascular. Integr Med (Encinitas), 20(4):34-38.[9] Also: Rosanoff A et al. (2021). Magnesium as a cofactor for vitamin D biosynthesis, transport, and activation. ScienceDirect. Systematic review (ResearchGate, Nov 2025) on the mechanistic synergy of D3, K2, and magnesium on skeletal metabolism confirmed complementary and additive effects across bone mineralisation pathways.

05. Vitamin C 250 mg rebuilds the collagen scaffold that holds muscle and bone together

After 40, collagen synthesis declines at approximately 1% per year, progressively weakening muscle fibres, tendons, ligaments, and bone matrix. Vitamin C is the irreplaceable cofactor for prolyl hydroxylase — the enzyme that crosslinks collagen strands into their functional triple-helix structure. Without adequate vitamin C, collagen is structurally defective and prone to breakdown. At 250 mg — nearly 3x the RDA — this formulation provides both cofactor support for collagen synthesis and antioxidant protection against oxidative muscle damage.

Evidence: The triad of collagen, vitamin C, and vitamin E in aging: emerging roles in mood and psychological health, neurotrophic support, cognitive function, endurance, and sarcopenia. Front Nutr, 2026:1806863. Age-associated anabolic resistance and sarcopenia significantly impair muscle protein synthesis, attributable in part to deterioration in muscle quality and alterations in extracellular matrix structure, including collagen. [10] Also: Vitamin C-enriched gelatin supplementation before intermittent activity augments collagen synthesis. Am J Clin Nutr, 105(1):136-143.[11]

06. Zinc 10 mg supports the anabolic signalling pathways that maintain muscle mass

Zinc is required for the synthesis and release of insulin-like growth factor-1 (IGF-1) — one of the primary anabolic hormones that drives muscle protein synthesis and opposes sarcopenia. It is also essential for testosterone metabolism, immune regulation, and antioxidant defence through superoxide dismutase (SOD). At 10 mg, close to the RDA of 8-11 mg/day and well below the 40 mg upper limit, this formulation corrects the zinc insufficiency common in adults over 40.

Evidence: The role of zinc on nutritional status, sarcopenia, and frailty in older adults: a scoping review. J Nutr Sci. Older adults with sarcopenia consistently showed poor zinc status related to loss of muscle mass and function. Zinc deficiency may further promote sarcopenia by interfering with antioxidant responses and autophagy. Also: The immune system and the impact of zinc during aging. Immun Ageing, 6:9.[12]

07. Vitamin B12 250 mcg combats homocysteine-driven muscle and bone deterioration

Elevated homocysteine is a recognised but underappreciated driver of musculoskeletal decline, impairing collagen crosslinking in bone and reducing muscle strength and physical performance. Vitamin B12 deficiency is particularly prevalent in adults over 50 due to reduced gastric acid and intrinsic factor, and in people using proton pump inhibitors or metformin. The 250 mcg dose ensures adequate absorption via passive diffusion even when active transport is impaired.

Evidence: Associations of serum vitamin B12 and its biomarkers with musculoskeletal health in middle-aged and older adults. Front Endocrinol, 15:1387035. Serum B12 was positively correlated with total appendicular lean mass (beta=584.83, P=0.044) in adults over 65. Plasma homocysteine was inversely associated with lean mass, gait speed, and knee extensor strength (all P<0.05).[13] Also: Relationship Between Plasma Homocysteine and Bone Density, Lean Mass, Muscle Strength in 1,480 Adults: NHANES. Calcif Tissue Int. [14]

08. Vitamin B1 25 mg fuels the mitochondrial energy production that powers every muscle contraction

Thiamine (B1) is an essential cofactor for pyruvate dehy-

drogenase and alpha-ketoglutarate dehydrogenase — two enzymes central to mitochondrial ATP production. Declining mitochondrial function is a key driver of age-related muscle weakness independent of muscle mass loss. B1 also plays a role in nerve conduction, supporting the neuromuscular signalling that coordinates muscle activation. Population data from NHANES linked B1 intake to early-onset sarcopenia prevalence.

Evidence: Association between dietary vitamin B1 and B2 intake and early-onset sarcopenia in the general adult US population: NHANES. Front Nutr. Identified significant inverse associations between B1 and B2 intake and sarcopenia prevalence in the adult US population.[15] Also: [16] The Impact of Nutritional Supplements on Sarcopenia: A Systematic Review and Meta-Analysis. Cureus. Vitamin B12 and B-complex vitamins were among the key nutrients analysed for impact on muscle mass and strength in sarcopenia patients.

09. Boron 3 mg reduces calcium and magnesium loss, raises free testosterone, and amplifies the formulation's mineral economy

Boron acts as a mineral conservator — it significantly reduces the urinary excretion of calcium and magnesium, meaning more of what is consumed from diet and supplementation is retained in bone. It also modulates sex hormone-binding globulin (SHBG), raising free testosterone levels in both men and women — a key anabolic signal for muscle mass maintenance. At 3 mg, it sits within the well-tolerated therapeutic range and far below the 20 mg/day upper limit.

Evidence: Effect of dietary boron on mineral, estrogen, and testosterone metabolism in postmenopausal women. FASEB J, 1(5):394-397. Boron supplementation markedly reduced urinary calcium and magnesium excretion and significantly elevated serum 17-beta-oestradiol and testosterone — changes expected to benefit bone density.[17] Also: SupplementScience (2026). Boron: Research & Evidence. Boron supplementation significantly increased free testosterone levels and reduced SHBG; the increase in free testosterone is biologically meaningful for muscle performance.

10. ch-OSA (Silicon) 6 mg simultaneously stimulates osteoblasts and suppresses osteoclasts — a dual bone-protective action unique in this formulation

Choline-stabilised orthosilicic acid (ch-OSA) is the only bioavailable form of silicon — dietary silicon in most foods is poorly absorbed. ch-OSA uniquely both stimulates bone-building cells (osteoblasts) and suppresses bone-resorbing cells (osteoclasts), providing dual action on the bone remodelling cycle. It is the most scientifically distinctive ingredient in this formulation, working through a completely different mechanism to every other mineral included.

Evidence: Orthosilicic acid inhibits human osteoclast differentiation and bone resorption. PLOS ONE, 19(10):e0312169. Published Oct 2024.[18] Also: [19] Choline-stabilised orthosilicic acid supplementation as an adjunct to Calcium/Vitamin D3 stimulates markers of bone formation in osteopenic females: a randomised, placebo-controlled trial. BMC Musculoskelet Disord, 9:85. King's College London RCT: participants receiving 6-12 mg Si showed greatest improvements in bone formation biomarkers.

11. ch-OSA and Vitamin C form a complementary pair for collagen synthesis — addressing the full biosynthetic pathway

Silicon acts upstream of vitamin C in collagen synthesis — it activates the genes that produce collagen type 1 in osteoblasts and fibroblasts, while vitamin C then crosslinks the collagen strands into functional fibres. Together, they address the full collagen biosynthetic pathway from gene expression through to structural maturation. This complementary pairing means the two ingredients work in sequence to rebuild the collagen scaffold that declines with age in both bone and muscle.

Evidence: Orthosilicic acid stimulates collagen type 1 synthesis and osteoblastic differentiation in human osteoblast-like cells in vitro. Bone, 32(2):127-135. Silicon directly stimulated collagen type 1 mRNA expression and prolyl hydroxylase activity.[20] Also: Dietary silicon intake positively associated with bone mineral density in men and premenopausal women of the Framingham Offspring Cohort: J Bone Miner Res, 19(2):297-307.[21]

12. The combination targets all five biological drivers of osteosarcopenia simultaneously

The five main pathological processes driving bone and muscle loss after 40 are: (1) declining anabolic hormone signalling [addressed by boron and zinc]; (2) rising inflammatory cytokines [addressed by vitamin D, C, and magnesium]; (3) declining collagen synthesis [addressed by ch-OSA and vitamin C]; (4) impaired calcium regulation [addressed by vitamin D, K2, and magnesium]; (5) elevated homocysteine [addressed by B12 and B1]. This formulation addresses all five pathways in a single daily dose — a level of multi-pathway coverage rarely achieved by a single supplement.

Evidence: A Narrative Review of the Evidence Supporting Nutritional Supplementation for Better Muscle Health in Older Adults. OBM Geriatrics, 9(1):296.[22] Also: Healthy Dietary Patterns and Risk of Sarcopenia in Adults Aged >50 Years. Nutrients. Vitamins D, C, E, and B-complex, as well as minerals including calcium, magnesium, and selenium,

support muscle function by promoting protein turnover, combating oxidative stress, and modulating inflammation.[24]

13. A 2025 systematic review and meta-analysis directly validates the core nutrients in this formulation

The most comprehensive recent synthesis of the evidence specifically covers the key nutrients in this formulation — vitamin D, B12, zinc, magnesium, and combinations thereof — in the context of sarcopenia treatment and prevention. The review confirmed that these nutrients improve body composition, muscle mass, strength, and physical function outcomes. It also found that combining nutritional intervention with resistance exercise further enhances clinical outcomes.

Evidence: The Impact of Nutritional Supplements on Sarcopenia: A Systematic Review and Meta-Analysis. Cureus, 17(7). 28 studies included. Nutritional interventions using protein, vitamin D, amino acids, omega-3, creatine, magnesium, zinc, and vitamin B12 were analysed for impact on muscle mass, strength, body composition and physical function. All core minerals in this formulation appeared in the positive evidence base.[24]

14. All nine ingredients are dosed within established safe limits with no clinically significant intra-formula interactions

Each ingredient is within safe upper limits: Vitamin D 2,000 IU (UL 4,000 IU); Magnesium Bisglycinate 140 mg elemental (UL 350 mg supplemental — the bisglycinate chelate form was selected for its superior gastrointestinal tolerability, with clinical studies confirming near-elimination of the laxative and cramping side effects associated with oxide and citrate forms at comparable elemental doses); Zinc 10 mg (UL 40 mg); Vitamin C 250 mg (UL 2,000 mg); Vitamin B12 250 mcg (water-soluble, no UL); Vitamin B1 25 mg (water-soluble, no UL); Vitamin K2 100 mcg (no established UL at this dose); Boron 3 mg (UL 20 mg); ch-OSA 6 mg (no established UL at therapeutic doses). One important clinical note: Vitamin K2 has a moderate interaction with warfarin (vitamin K antagonists) and must be disclosed on labelling. People on direct oral anticoagulants (DOACs) are not significantly affected.

Evidence: NIH Office of Dietary Supplements Fact Sheets (2024): Vitamin D, Magnesium, Zinc, Vitamin C, Vitamin B12, Vitamin B1, Vitamin K — tolerable upper intake levels. EFSA (2012). Scientific Opinion on Tolerable Upper Intake Level of Boron. EFSA Journal, 11(11):3185. Also: Drugs.com (2024). Vitamin K2 — Warfarin Interaction Summary. A moderate drug interaction exists between Vitamin K2 and Warfarin; K2 can lower INR, requiring monitoring and dose adjustment in anticoagulated patients.[23]

15.This formulation uniquely targets both bone and muscle through shared biological pathways — osteosarcopenia as a unified clinical target

Most supplements target either bone (calcium, vitamin D) or muscle (protein, creatine) in isolation. This combination is designed around osteosarcopenia — the co-occurrence of bone and muscle loss that accelerates after 40, driven by shared hormonal, inflammatory, and nutritional pathways. By combining nutrients that act on bone mineralisation, collagen matrix integrity, muscle anabolism, mitochondrial energy, and homocysteine regulation, this formulation addresses both tissues through their common biology — making it mechanistically coherent as a dual bone-and-muscle protective strategy.

Evidence: Beyond Calcium and Vitamin D: Exploring Creatine, beta-Hydroxy-beta-methylbutyrate, Prebiotics and Probiotics in Osteosarcopenia. Nutrients, PMC12300471. Nutritional interventions for osteosarcopenia play a pivotal role in not only improving bone and muscle composition but also enhancing functional outcomes in older adults.[2] Also: [1] Osteosarcopenia: epidemiology, diagnosis, and treatment — facts and numbers. J Cachexia Sarcopenia Muscle, 11(3):609-618.

2,000 IU Vitamin D3	250 mg Vitamin C	140 mg Magnesium Bisglycinate
10 mg Zinc	25 mg Vitamin B1	250 mcg Vitamin B12
3 mg Boron	100 mcg Vitamin K2 (MK-7)	6 mg ch-OSA Silicon

can help preserve muscle and bone health in adults over the age of 40

How the combination of Vitamin D 2,000 IU

- Vitamin C 250 mg
- Magnesium Bisglycinate 140 mg
- Zinc 10 mg
- Vitamin B1 25 mg
- Vitamin B12 250 mcg
- Boron 3 mg
- Vitamin K2 (MK-7) 100 mcg
- Choline-Stabilised Orthosilicic Acid 6 mg

Important Safety Note:

Individuals taking warfarin (a vitamin K antagonist) should not start this formulation without medical supervision, as the

Vitamin K2 content has a moderate interaction with warfarin and may alter INR. People on direct oral anticoagulants (DOACs such as apixaban or rivaroxaban) are not significantly affected.

People with moderate-to-severe renal impairment should consult a physician before use, as magnesium and boron are renally excreted. People with hormone-sensitive conditions should discuss boron supplementation with their doctor due to its modest effect on oestrogen and testosterone levels.

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Citation: Usman Mansoor, Dr Adeel Chaudhary, Dr Maaza Usman, Muscle & Bone Health After 40, *J. Food Nutr.* Vol 5, Iss 2. (2026). DOI: 10.58489/2836-2276/048