Nutrition, Physical Activity, and Bone Health in Women

Richard D. Lewis and Christopher M. Modlesky

Calcium and vitamin D can significantly impact bone mineral and fracture risk in women. Unfortunately, calcium intakes in women are low and many elderly have poor vitamin D status. Supplementation with calcium (~1000 mg) can reduce bone loss in premenopausal and late postmenopausal women, especially at sites that have a high cortical bone composition. Vitamin D supplementation slows bone loss and reduces fracture rates in late postmenopausal women. While an excess of nutrients such as sodium and protein potentially affect bone mineral through increased calcium excretion, phytoestrogens in soy foods may attenuate bone loss through estrogenlike activity. Weight-bearing physical activity may reduce the risk of osteoporosis in women by augmenting bone mineral during the early adult years and reducing the loss of bone following menopause. High-load activities, such as resistance training, appear to provide the best stimulus for enhancing bone mineral; however, repetitive activities, such as walking, may have a positive impact on bone mineral when performed at higher intensities. Irrespective of changes in bone mineral, physical activities that improve muscular strength, endurance, and balance may reduce fracture risk by reducing the risk of falling. The combined effect of physical activity and calcium supplementation on bone mineral needs further investigation.

Key Words: calcium, vitamin D, exercise, bone mineral, osteoporosis

During the next decade, an estimated 5.2 million osteoporotic fractures are projected to occur in Caucasian American postmenopausal women, with direct costs of ~$45.2 billion (25). Low levels of bone mineral and microarchitectural deterioration of bone tissue are key factors that increase fracture risk (27, 63). Two measures of bone mineral include bone mineral content (BMC) or bone mass, the absolute amount of hydroxyapatite or calcium phosphate crystal present in bone, and bone mineral density (BMD), the relative amount of BMC in a given area of bone. The World Health Organization (WHO) developed diagnostic criteria for osteopenia (low bone mineral) and osteoporosis based on BMD measures (158). A BMD measure of 1–2.5 standard deviations (SD) below the normal value for young adults is considered osteopenic and more than 2.5 SD below normal is considered osteoporotic (75). Heaney (63) estimated that for every 1 SD decline in BMD,

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fracture risk increases two to three times. Based on the WHO criteria, Melton (102) reported that 16.8 million (54%) and 9.4 million (30%) postmenopausal Caucasian women in the U.S. have osteopenia and osteoporosis, respectively.

To fully appreciate the role of nutrition and physical activity in osteoporosis prevention, it is essential to understand the makeup and functions of the skeleton. Bone is a dynamic organ composed of minerals, primarily calcium and phosphorus, in the form of hydroxyapatite enmeshed in a matrix of collagenous and noncollagenous proteins (46). Throughout the lifecycle bone is constantly turning over, a process called remodeling. Bone remodeling is the coupled or linked activation of resorption and formation occurring at the same anatomical site, with 15 to 20% of the total skeleton undergoing remodeling at any one time (75). The two types of bone cells responsible for this linked process are osteoclasts, bone resorbing cells, and osteoblasts, bone forming cells (46). Following activation of the remodeling cycle, osteoclasts initiate bone resorption and osteoblasts subsequently promote filling of the cavity with matrix. Mineralization of the matrix completes the remodeling cycle approximately 9 months from initiation. During menopause and estrogen withdrawal, the number of remodeling sites activated is increased and the rate of resorption increases to a greater extent than formation. As a result of the imbalance between resorption and formation, calcium is released from the skeleton and bone mineral is reduced (75). Type I (menopausal) osteoporosis is characterized by estrogen withdrawal, accelerated bone turnover, and marked liberation of bone mineral (53).

Trabecular bone, a soft spongy bone comprised of horizontal and vertical cross-links, has a large surface area and is susceptible to accelerated bone turnover. The axial skeleton, which has a large trabecular makeup, is primarily affected by estrogen withdrawal. In contrast, cortical bone, which makes up 80% of the total skeletal mass, is found primarily in the shafts of the long bones, such as the femoral shaft, of the peripheral skeleton and is less responsive to estrogen withdrawal.

In addition to the obvious structural role of the skeleton, bone serves as a reservoir of calcium for the extracellular fluid, such that calcium is constantly being exchanged between bone and plasma. There is tight regulation of calcium within extracellular fluid by parathyroid hormone (PTH), calcitonin, and vitamin D (Figure 1). During a state of calcium insufficiency, PTH and 1,25-dihydroxycholecalciferol (1,25(OH)₂D₃) levels are elevated and cause increased bone resorption, increased efficiency of calcium absorption, decreased excretion of calcium, and normalization of blood calcium levels. Secondary hyperparathyroidism, which is age related, has been identified as a determinant of bone loss in Type II or senile osteoporosis (53).

Recommended strategies for reducing fracture risks are to maximize peak bone mass (PBM) and to slow or prevent bone loss associated with estrogen withdrawal during the postmenopausal years. Whole body, lumbar spine, and forearm PBM are thought to occur sometime during the third decade of life. Matkovic et al. (98) suggested that femoral neck BMD peaks sometime during late adolescence. Although the premenopausal years are characterized by small changes in BMD, the rate of BMD loss is approximately 3% per year during the first 5 years following the onset of menopause and approximately 1% per year thereafter (31). Menopause is the natural cessation of menstruation, which typically occurs during the fifth or sixth decade of life. Perimenopause is a 3- to 5-year period preceding menopause during which estrogen levels begin to decrease without cessation of menstruation.
Figure 1 — Schematic representation of the hormonal control loop for vitamin D metabolism and function. A reduction in the serum calcium below approximately 2.09 mM/L (8.8 mg/dL) prompts a proportional increase in the secretion of parathyroid hormone, which enhances the mobilization of calcium stores from bone. Parathyroid hormone also promotes the synthesis of 1,25(OH)₂D in the kidney, which in turn mobilizes calcium from the bone and intestine. © J. Nutr. 126:1159S-1164S, 1996. American Society for Nutritional Sciences.

Multiple factors including genotype, diet, physical activity, and reproductive–endocrine status have the potential to significantly impact BMD and, ultimately, fracture risk (Figure 2). Nutrients have the potential to influence bone either through the regulation of calcium balance (i.e., calcium, vitamin D, sodium, phosphorus) or through synthesis and degradation of the extracellular matrix (i.e., copper, zinc). The potential benefits of calcium and vitamin D supplementation in adult and elderly females are linked to the homeostatic mechanisms for maintaining calcium balance and reducing bone turnover via PTH (6, 101, 103, 116). The purpose of this review is to determine the role of nutritional factors, most notably, calcium and vitamin D, and physical activity in the maintenance of BMD and their utility in the prevention of osteoporotic fractures in premenopausal, perimenopausal, and early and late postmenopausal women.
Calcium Intake

**Premenopausal Women**

There appears to be agreement that the BMD response to higher intakes or supplementation of calcium is more robust during childhood and adolescence, a critical period for optimizing PBM (74, 88, 89), provided that the higher calcium intake is maintained (87). Additionally, historical or past calcium intake has been identified as a key determinant of bone mass in young women (57, 137, 150). However, uncertainty still exists with respect to the relationship of calcium intake to BMD in premenopausal women and the benefits of calcium supplementation. Numerous cross-sectional studies have reported mixed results regarding the relationship between current calcium intake and BMD in young women. However, using strict inclusion criteria in a meta-analysis of 24 cross-sectional studies, Welten et al. (156) concluded that there was a small significant positive relationship between calcium intake and BMD in premenopausal women.

**Prospective Observational Studies.** Prospective observational studies are also inconclusive regarding the relationship between calcium and BMD during the premenopausal years (100, 122, 128). In a 5-year study of 156 college-aged women, Recker et al. (122) found that bone gain in the lumbar spine, forearm, and whole body occurred by the third decade and that lumbar spine BMD gain was positively related to the calcium/protein intake ratio, determined from 7-day food records. Mazess and Barden (100), who observed little change in BMD at any site over 2 years in 200–300 women 20–39 years of age, reported that body mass, not calcium intake, was the best predictor of BMD. The authors used two 24-hr food records per year to estimate calcium intake, which may not be enough days to provide a reliable measure of calcium intake. Riggs et al. (128), like Mazess and Barden (100), did not observe a significant relationship between calcium intake and lumbar spine and midradius BMD in a smaller group of women (N = 45, 25–55 years of age) over 2.5 years. The relationship between calcium and BMD in older premenopausal women may be complicated by small changes in BMD. In older premenopausal women nearing menopause, bone loss of approximately 1% was observed during a 1-year period at the lumbar spine, whole body, and forearm (122).
Table 1  Calcium and Vitamin D Recommendations for Adult and Elderly Females

<table>
<thead>
<tr>
<th></th>
<th>Calcium (mg/day)</th>
<th>Vitamin D (IU/day)</th>
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<tbody>
<tr>
<td></td>
<td>AI</td>
<td>NIH</td>
</tr>
<tr>
<td>19–24 years</td>
<td>1,000</td>
<td>1,200–1,500</td>
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<tr>
<td>25–50 years</td>
<td>1,000</td>
<td>1,000</td>
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<tr>
<td>Pregnant and lactating</td>
<td>1,000</td>
<td>1,200–1,500</td>
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<tr>
<td>(19–50 years)</td>
<td></td>
<td></td>
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<tr>
<td>Postmenopausal w/ERT</td>
<td>1,000</td>
<td></td>
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<tr>
<td>Postmenopausal w/out ERT</td>
<td>1,200\textsuperscript{a}</td>
<td>1,500</td>
</tr>
<tr>
<td>Women &gt;65 years</td>
<td>1,200\textsuperscript{a}</td>
<td>1,500</td>
</tr>
</tbody>
</table>

\textsuperscript{a}AI = Adequate Intake, 1997. \textsuperscript{b}NIH = National Institutes of Health Consensus Conference, 1994. \textsuperscript{c}ERT = estrogen replacement therapy. \textsuperscript{d}Al = 51–70 years and >70 years = 1,200 mg Ca/day. \textsuperscript{e}Al = 51–70 years = 400 IU/day; >70 years = 600 IU/day.

Mean calcium intakes in the studies by Mazess and Barden (100), Recker et al. (122), and Riggs et al. (128) were 909 ± 351, 781 ± 300, and 922 ± 355 mg/day, respectively, lower than the recommendations by the National Academy of Science and the National Institutes of Health (NIH; Table 1). While these levels of intake appear adequate for maintenance of bone mineral in young and older premenopausal women, they could potentially limit PBM attainment.

**Intervention Trials.** Several intervention studies support increased calcium intake to prevent site-specific bone loss during the premenopausal and perimenopausal years (8, 44, 45, 127, 140). Using a nonrandomized, double-blind, placebo-controlled design, Rico et al. (127) found that calcium supplementation of 1,000 mg/day for 1 year increased total body bone mineral by 2.6% in premenopausal women consuming ~700 mg/day. In a double-blind, placebo-controlled trial, supplementation with 1,500 mg/day of calcium significantly attenuated BMC loss at the left humerus in 42-year-old premenopausal women (~0.62%) compared to controls (~1.53%) (140). No benefit of calcium supplementation was observed at the radius or ulna. In women 30–42 years of age, increasing calcium consumption with dairy products from ~900 mg/day to ~1,500 mg/day for 3 years prevented loss of vertebral BMD compared to nonsupplemented women (~0.4 ± 0.9% vs. ~2.9 ± 0.8%) (8).

Similarly, Elders et al. (44, 45) demonstrated that calcium supplementation (1,000 or 2,000 mg/day) in premenopausal and perimenopausal women consuming ~1,000 mg/day significantly prevented lumbar spine bone loss over 3 years (Figure 3). Women in the control group lost 3.2% compared to the calcium-supplemented subjects, who lost 1.6%. The initial year of the study was the most pronounced in terms of the calcium effect on the rate of lumbar spine bone loss. In fact, the rate of lumbar spine bone loss was similar between the groups following the first year of the study.

Agents such as calcium inhibit activation of the remodeling cycle, thus decreasing the rate of resorption; this was demonstrated by Scopacasa et al. (138), who found that short-term administration of 1,000 mg of calcium significantly reduced urinary excretion of hydroxyproline, pyridinoline, and deoxypyridinoline. Accordingly, the first few months of supplementation are characterized by a greater degree
of bone mineral deposition than bone resorption, increasing BMD and BMC. After
the first remodeling cycle is completed, however, rates of resorption and mineral-
ization are once again matched, and further increases in bone mineral may not be
observed (62). Calcium supplementation on the order of 1,000 mg/day in women
consuming 700–1,000 mg calcium/day appears to help maintain bone and prevent
premenopausal bone loss.

Postmenopausal Women

There is substantial evidence that long-term estrogen replacement therapy (ERT)
prevents bone loss and decreases the risk of osteoporotic fractures in postmenopausal
women (75). The standard dose of estrogen is typically 0.625 mg. However, not all
early postmenopausal women elect to subscribe to years of ERT. Three questions
regarding calcium supplementation and bone mass during the postmenopausal years
need to be addressed: What are the effects of calcium supplementation on bone
during a period of rapid bone loss? Can calcium supplementation substitute for
estrogen in slowing or preventing menopausal bone loss? If women elect to sub-
scribe to estrogen therapy, can calcium supplementation augment the effects of
estrogen on bone? To answer these questions, it is important to examine early and
late postmenopause separately.

Early Postmenopause. During the first 5 years of menopause, estrogen levels
drop dramatically, thus increasing bone turnover, bone resorption, and release of
calcium from bone and decreasing efficiency of calcium absorption (64, 75). Earlier
it was hypothesized that because calcium absorption is decreased during early
menopause, higher intakes of calcium may be necessary. However, because osteo-
clast activity increases and calcium release from the skeleton is accelerated, the
beneficial effects of calcium supplementation on bone in early postmenopausal
women are modest (Table 2). Riis et al. (129) found that calcium supplementation
<table>
<thead>
<tr>
<th>Author</th>
<th>Subject age (years)</th>
<th>Menopausal age (years)</th>
<th>n</th>
<th>Design</th>
<th>Supplement</th>
<th>ERT</th>
<th>Duration (years)</th>
<th>Dietary calcium/day</th>
<th>BMD sites measured</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Riis et al. (129)</td>
<td>50.0 ± 0.5 (placebo)</td>
<td>1.3 ± 0.2</td>
<td>220</td>
<td>R, PC, DB</td>
<td>2,000 mg CC or 3 mg 17β-estradiol</td>
<td>No previous use</td>
<td>2</td>
<td>NR</td>
<td>Proximal &amp; distal forearm, spine, whole body</td>
<td>Calcium not as effective as estrogen. Calcium did slow loss in proximal forearm.</td>
</tr>
<tr>
<td>Dawson-Hughes et al. (33)</td>
<td>54.5 ± 3.4 (early PM)</td>
<td>3.2 ± 1.4 and 13.0 ± 5.6</td>
<td>236</td>
<td>R, PC, DB</td>
<td>500 mg of CC or CCM</td>
<td>No previous use</td>
<td>2</td>
<td>&lt;400 mg or 400–650 mg</td>
<td>Spine, radius, femoral neck</td>
<td>Spine ↓ significantly in all groups. No effect of calcium in early PM women. CCM slowed bone loss at LS, FN and R in low calcium consumers.</td>
</tr>
<tr>
<td>Elders et al. (44)</td>
<td>50.1 ± 7.9 (controls)</td>
<td>&lt;3 years</td>
<td>129</td>
<td>R</td>
<td>1,000 or 2,000 mg of a combination of CLG and CC</td>
<td>No previous use</td>
<td>3</td>
<td>1,000 mg for all groups</td>
<td>Spine, metacarpal cortical thickness</td>
<td>Calcium supplement did not prevent spine bone loss. MCT ↓ 3% in controls and 2% in 1,000 mg suppl. Bone turnover ↓ with suppl.</td>
</tr>
<tr>
<td>Study</td>
<td>Calcium Dose</td>
<td>N</td>
<td>Design</td>
<td>Duration</td>
<td>Treatment Details</td>
<td>Site(s)</td>
<td>Notes</td>
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<tr>
<td>Aloia et al. (4)</td>
<td>52.8 ± 3 (placebo) 51.3 ± 2 (calcium) 51.2 ± 2.8 (estrogen)</td>
<td>101</td>
<td>R, PC</td>
<td>1.6–2.0</td>
<td>600 mg CC or 0.625 mg/daily estrogen; both groups received 400 IU Vit D</td>
<td>Whole body, spine, radius, neck, Ward's triangle, trochanter</td>
<td>Calcium less effective than estrogen. Calcium slowed bone loss from FN and whole body. No effect on spine or other sites.</td>
<td></td>
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<tr>
<td>Cepollaro et al. (19)</td>
<td>52.3 ± 2.1 (high calcium) 52.9 ± 1.0 (low calcium)</td>
<td>45</td>
<td>R, PC</td>
<td>1.4 ± 8</td>
<td>400 mg calcium bicarbonate in mineral water</td>
<td>Distal radius, osteocalcin</td>
<td>Calcium suppl. significantly reduced osteocalcin and bone loss at DR</td>
<td></td>
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<tr>
<td>Smith et al. (140)</td>
<td>55.1 ± 4.6 (control) 55.0 ± 4.8 (treatment)</td>
<td>82</td>
<td>R, DB, PC</td>
<td>6.1 ± 5 and 7.3 ± 8</td>
<td>1,500 mg CC</td>
<td>No previous use</td>
<td>4</td>
<td>~700 mg for both groups</td>
<td>Radius, humerus</td>
<td>Calcium suppl. significantly reduced bone loss at the humerus, ulna, and radius.</td>
</tr>
<tr>
<td>Nelson et al. (106)</td>
<td>60.2 ± 1.1 (controls and calcium)</td>
<td>36</td>
<td>R, DB, PC</td>
<td>10.8 ± 1.2</td>
<td>831 mg/day in milk drink</td>
<td>No previous use</td>
<td>1</td>
<td>~850 mg for all groups</td>
<td>Spine, femur, radius, total body</td>
<td>FN BMD ↑ in suppl. and ↓ in placebo groups. Difference was significant. No effect on spine.</td>
</tr>
<tr>
<td>Chevalley et al. (23)</td>
<td>72 ± 0.6 (no history of fracture) 78.4 ± 1 (history of fracture)</td>
<td>93</td>
<td>R, PC, DB</td>
<td>22.5 ± 1 and 29.5 ± 1.2</td>
<td>800 mg/day osseino-mineral complex or calcium carbonate</td>
<td>No previous use</td>
<td>1.5</td>
<td>619 ± 33 (no history of fracture) 594 ± 39 (history of fracture)</td>
<td>Femoral shaft, femoral neck, lumbar spine, fracture rate</td>
<td>Calcium lowered vertebral fracture rate and femoral shaft BMD loss.</td>
</tr>
<tr>
<td>Study</td>
<td>Baseline (placebo)</td>
<td>Baseline (calcium)</td>
<td>Participants</td>
<td>Protocol</td>
<td>Dose</td>
<td>Outcome</td>
<td>Notes</td>
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<tr>
<td>Reid (125)</td>
<td>59 ± 6 (placebo)</td>
<td>58 ± 4 (calcium)</td>
<td>78</td>
<td>R, PC, DB</td>
<td>1,000 mg</td>
<td>CLG CC</td>
<td>No previous use</td>
<td>Whole body, spine, femoral neck, Ward's triangle, trochanter</td>
<td>Calcium reduced LS bone loss in year 1, but not thereafter. Rates of whole body BMD loss are less in calcium group vs. control over 4 years.</td>
<td></td>
</tr>
<tr>
<td>Prince et al. (117)</td>
<td>63 ± 4 (placebo)</td>
<td>62 ± 5 (calcium)</td>
<td>168</td>
<td>R, DB, PC</td>
<td>1,000 mg calcium from milk powder or 1,000 mg as CLG</td>
<td>No previous use</td>
<td>2</td>
<td>~800 mg</td>
<td>Femoral neck, trochanter, total hip, intertrochanteric, lumbar spine, tibia</td>
<td>Calcium suppl. prevented or slowed bone loss at trochanter, intertrochanter, and ultradistal radius. No effect on spine.</td>
</tr>
<tr>
<td>Fujita et al. (52)</td>
<td>82</td>
<td>NR</td>
<td>58</td>
<td>R, DB, PC Hospitalized subjects</td>
<td>900 mg of either OS calcium or CC</td>
<td>NR</td>
<td>1.5</td>
<td>NR</td>
<td>Lumbar spine, whole body</td>
<td>Calcium suppl., OS CaCo, prevented BMD loss over 1.5 years. Intact PTH lower in OS vs. placebo.</td>
</tr>
<tr>
<td>Devine (37)</td>
<td>Follow-up to Prince et al. (1995) (117)</td>
<td>66 ± 1</td>
<td>84</td>
<td>PC</td>
<td>1,000 mg</td>
<td>CLG</td>
<td>No previous use</td>
<td>Same as Prince et al. (1995) (117)</td>
<td>Calcium suppl. continued to significantly prevent bone loss at hip and ankle. No observed loss at spine in either group.</td>
<td></td>
</tr>
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</table>

R = randomized; PC = placebo controlled; DB = double blind; LS = lumbar spine; FN = femoral neck; DR = distal radius; CLG = calcium lactate gluconate; CCM = calcium citrate malate; CC = calcium citrate; NR = not reported; MCT = metacarpal cortical thickness; PM = postmenopausal; OS = oyster shell; suppl. = supplement.
(2,000 mg) for 2 years in women with a menopausal age of 1–2 years slowed bone loss in the proximal forearm but not in the lumbar spine. On the other hand, ERT resulted in significant improvements at both sites. Similarly, Dawson-Hughes (33), Elders et al. (44) (Figure 3), and Aloia et al. (4) found that calcium supplementation did not prevent spine bone loss. Nonetheless, Elders et al. (44) found the loss of metacarpal cortical bone to be somewhat lower (∼1%) with supplementation and Aloia et al. (4) reported a slowing of bone loss in the femoral neck and whole body. More recently, Cepollaro et al. (19) reported that calcium supplementation for 13 months taken with mineral water significantly slowed bone loss at the distal radius in early postmenopausal women. Based on the available evidence it appears as though the attenuating effect on bone loss previously reported (4, 19, 44, 129) is small and appears to be in bone sites of primarily cortical bone (Table 2). Because the spine is predominantly trabecular bone and more responsive to estrogen withdrawal, calcium supplementation cannot override this powerful effect (61).

**Calcium and Estrogen.** Several researchers in addition to Riis et al. (129) have compared the BMD response to estrogen use, calcium supplementation, or a combination of the two (4, 29, 56, 129). The evidence seems unequivocal that ERT, at a dose of ∼0.625 mg/day of conjugated estrogens, is more effective at preserving bone mass than calcium supplementation (4, 29, 129). When calcium supplementation is combined with ERT there appears to be an augmented effect at the femoral neck and whole body, but not at other sites (29, 56). The maximal BMD effect of ERT combined with calcium supplementation occurs in women with low calcium intakes (29, 56, 60). Hence, in order to maximize the benefits of ERT on bone preservation, adequate intakes of calcium are required (60).

**Estrogenlike Compounds.** Interestingly, soy food products contain phytoestrogens, isoflavones, and coumestans, compounds hypothesized to improve bone health through their estrogenlike actions (39). Coumestrol (coumestan), genistein, and daidzein (isoflavones) in soy are similar in structure to estrogen and bind to estrogen receptors (39). While there are limited data on the effects of soy on bone, Arjmandi et al. (7) reported that soy-fed ovariectomized rats had greater vertebral and femoral bone densities than non-soy-fed ovariectomized rats. Furthermore, the higher vertebral bone density in the soy-fed rats was similar to the bone response in a separate group of ovariectomized rats treated with estrogen. It was not clear, however, what specific compound in soy was responsible for the elevated bone densities. More recently, Draper and coworkers (39) reported that ovariectomized rats injected with coumestrol (1.5 mmol twice per week) had significantly less ovariectomy-induced bone loss at the femur, whole body, and spine. Bone loss was not prevented in ovariectomized rats treated with isoflavone, suggesting a specific bone health benefit of the coumestans. Currently, human studies are under way to provide further insight into this interesting hypothesis.

**Late Postmenopause.** There is increasing concern regarding chronic calcium insufficiency in older postmenopausal women and the subsequent risks for debilitating fractures. For postmenopausal women (>6 years since menopause), evidence supports the notion that calcium supplementation (∼500–1,500 mg/day) significantly slows bone loss in women consuming levels of calcium lower than recommended by the NIH (33, 37, 52, 117, 125, 140) (Table 2). This response is most evident in cortical bone sites such as the humerus (140), radius (33, 140), and femur (23, 33, 37, 117). Beneficial effects of calcium supplementation on spine bone loss have been reported but are less pronounced. Prince et al. (117) and Devine et al. (37) found that calcium supplementation (1,000 mg) had no effect on spine
BMD over periods of 2 and 4 years, respectively. In fact, the authors did not observe bone loss at the spine in any subject groups. In contrast, Dawson-Hughes et al. (33) and Fujita et al. (52) both found that calcium supplements in the forms of calcium citrate malate and oyster-shell calcium, respectively, prevented bone loss at the spine. Reid et al. (125) also reported that 1,000 mg of a combination of calcium lactate gluconate and calcium carbonate significantly slowed the rate of spine bone loss after 1 year (1.7 ± 0.6% difference from placebo), but the rate of change was not different after 2 or 4 years of supplementation. The beneficial effect of calcium on the spine in the Dawson-Hughes et al. (33) study may be related to the low baseline calcium intakes of the subjects (<400 mg/day), suggesting a possible threshold effect. Mean calcium intakes in the other studies were approximately 700 mg or higher. Additionally, the subjects studied by Fujita et al. (52) were considerably older and hospitalized, and there was no description of estrogen use or other subject exclusion criteria that might have influenced the results.

**Calcium and Fracture Rate.** While the annual benefit of calcium supplementation on bone loss may be small, the cumulative effect over several decades may be substantial and may significantly attenuate the fracture rate. Some prospective studies of elderly women suggest that higher calcium intakes reduce the risk for hip and spine fractures (70, 93, 117). Holbrook et al. (70) found that calcium intake, based on 24-hr recall, was inversely associated with hip fracture in 957 men and women, aged 50–79 years, who were followed for 12 years. Looker et al. (93) followed 4,342 men and women, 50–74 years of age, who were part of the National Health Examination Survey I Epidemiological Follow-Up Study. Postmenopausal women >6 years past menopause and in the highest quartile of calcium intake had a 50% lower risk of experiencing a hip fracture than women in the lowest quartile. Two groups of elderly women (73.5 ± 7.1 years of age), one with a high prevalence of vertebral fractures and the other without fractures, both consuming less than 1,000 mg of calcium per day, were supplemented with 1,200 mg/day calcium carbonate or a placebo in a double-blind fashion (123). Women with prevalent fractures and receiving calcium did not lose forearm bone mass (2% higher than placebo) and had a reduced rate of fractures compared to placebo subjects. Calcium supplementation in the group with a low prevalence of fractures did not reduce the number of fractures.

Reid et al. (125) also found that calcium supplementation significantly reduced the fracture rate in postmenopausal women. Reid (124) suggested that the antifracture efficacy of calcium supplementation was surprising since the BMD changes after 4 years were only 1–4%. The dissociation between BMD and fracture rate may be due to the overall reduction in bone turnover (124) associated with suppression of high PTH levels (101). Additional studies are needed to confirm the finding of reduced fractures with long-term calcium supplementation.

**Other Nutrients.** Nutrients such as phosphorus, sodium, and protein may influence calcium availability and potentially impact bone mass (15, 32, 36, 97). High phosphorus intakes or low calcium–phosphorus ratios have been found to promote bone loss in animals and to impair the endocrine response to low calcium intakes in older adults; however, clinical trials are needed to assess the bone response in humans (15). Chronic overconsumption of sodium chloride increases urinary calcium and may contribute to bone loss (36). In a 2-year study in late postmenopausal women, increased urinary sodium was negatively correlated with changes in femur BMD (−192, p < .05) (36). Similarly, high protein intakes increase urinary calcium loss and potentially increase calcium needs (59, 64). It is possible that population groups with high sodium and/or high protein intakes have an increased
requirement for calcium; however, further work is needed to assess the relationships among sodium, protein, calcium, and bone mass in humans.

Calcium intakes that allow for the development of each person’s genetically programmed PBM and slow bone loss in the elderly continue to be investigated. An expert panel of the Food and Nutrition Board recently released new recommendations for calcium intakes, the Reference Dietary Intakes (RDIs) (48). The panel recommended that the Adequate Intakes (AIs), one category within the RDIs that takes into account disease risk reduction, should be 1,000 mg/day for women 19–50 years and 1,200 mg/day for those 51+ years. These values are more consistent with the recommendations issued by the NIH Consensus Conference Panel (112) (Table 1) for calcium intakes in adult and elderly females and appear to coincide with several studies cited above.

Unfortunately, according to the United States Department of Agriculture 1987–88 Nationwide Food Consumption Survey (47), the mean calcium intakes for American women 20+ years of age is approximately 590 mg/day. Additionally, women 19–80+ years of age from Phase I of the National Nutrition Examination Survey III (Figure 4) consume calcium at mean values lower than recommendations of the National Research Council, Food and Nutrition Board, RDIs (48), and the NIH Consensus Conference Panel (112) (Table 1).

**Vitamin D, Bone, and Fracture Rates**

Inadequate intakes of vitamin D, low sunlight exposure, diminished intestinal absorption, and reduced synthesis of active vitamin D contribute to poor vitamin D status in the elderly (51, 55, 71). Because of the role vitamin D plays with respect to calcium homeostasis and PTH regulation, poor vitamin D status in the elderly is associated with the development of osteoporosis (53, 91). Several recent studies have examined the impact of vitamin D supplementation on BMD and fracture rates in elderly women (22, 30, 34, 65, 91, 111) (Table 3). Dawson-Hughes et al. (32) found that during the winter months when 25-hydroxycholecalciferol (25(OH)D)

![Figure 4 — Mean calcium intakes ± SEM in women from NHANES III, Phase I, 1988-91. Adapted from Alaimo et al. (1).](image-url)
<table>
<thead>
<tr>
<th>Author</th>
<th>Subject age (years)</th>
<th>Fracture history</th>
<th>n</th>
<th>Design</th>
<th>Supplement</th>
<th>ERT</th>
<th>Duration (years)</th>
<th>Dietary calcium &amp; vit D/day</th>
<th>Outcome measures</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dawson-Hughes (30)</td>
<td>61.9 ± 0.5 (placebo) and 61.4 ± 0.5 (vitamin D)</td>
<td>No</td>
<td>249</td>
<td>R, DB, PC</td>
<td>400 IU vit. D₃; 377 mg calcium</td>
<td>No</td>
<td>1</td>
<td>~700 mg; ~100 IU</td>
<td>Spine, whole body</td>
<td>Spinal bone loss from December to June less in vit D-suppl. group.</td>
</tr>
<tr>
<td>Chapuy et al. (20,21)</td>
<td>84 ± 6 (placebo) 84 ± 6 (vitamin D-calcium)</td>
<td>Not excluded</td>
<td>3,270</td>
<td>R, PC</td>
<td>800 IU vit D₃, 1,200 mg tricalcium phosphate</td>
<td>Not an exclusion criteria</td>
<td>3</td>
<td>~500 mg</td>
<td>Fracture rate, femoral neck, total proximal femur, trochanter, intertrochanteric region, PTH, 25(OH)D₃</td>
<td>Suppl. ↓ incidence hip fractures by 43% and nonvertebral fracture by 32%. After 18 months, significant ↑ in femoral neck and total proximal femur. Significant ↓ in PTH and in 25 (OH)D₃.</td>
</tr>
<tr>
<td>Ooms et al. (111)</td>
<td>80.6 ± 5.5 (placebo) 80.1 ± 5.6 (vitamin D)</td>
<td>No</td>
<td>348</td>
<td>R, DB, PC</td>
<td>400 IU vit D₃</td>
<td>NR</td>
<td>2</td>
<td>~860 mg; NR for vit D</td>
<td>BMD: total femur, trochanter, distal radius, osteocalcin, 1,25 (OH), D₃, PTH, calcitonin</td>
<td>Vit D₃ suppl. resulted in slight ↑ 1,25(OH)D₃, ↓ PTH, and ↑ BM at femoral neck</td>
</tr>
<tr>
<td>Study</td>
<td>Design</td>
<td>Subjects</td>
<td>Treatment</td>
<td>Follow-up</td>
<td>Results</td>
<td></td>
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<tr>
<td>Dawson-Hughes et al. (35)</td>
<td>No</td>
<td>261</td>
<td>R, DB, PC, 100 IU or 700 IU vit D &amp; 500 mg calcium</td>
<td>Not within the year</td>
<td>2 *460 mg; ~110 IU Femoral neck, spine, whole body 700 IU slowed bone loss at femoral neck. No loss at spine.</td>
<td></td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Lips (91)</td>
<td>No</td>
<td>1,916</td>
<td>R, PC, DB, 400 IU vit D₃</td>
<td>Subjects using drugs that affect bone were not excluded</td>
<td>3.5 *860 mg; NR for vit D 25(OH)D₃ hip fracture, other nonvertebrae fractures No significant reduction in incidence of hip fractures.</td>
<td></td>
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</tr>
<tr>
<td>Dawson-Hughes et al. (34)</td>
<td>No</td>
<td>170</td>
<td>R, DB, PC, 700 IU vit.D₃, 500 mg CCM</td>
<td>No</td>
<td>3 ~689–798 mg; 174–184 IU Femoral neck, lumbar spine, total body, fracture rate Versus placebo, suppl. ↑ BMD at all sites at year 1. Difference significant only for total body at years 2 and 3. Fracture incidence reduced with suppl.</td>
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</table>

R = randomized; PC = placebo controlled; DB = double blind; LS = lumbar spine; FN = femoral neck; CCM = calcium citrate malate; NR = not reported; suppl. = supplement.
levels are lower and PTH higher, supplementation with vitamin D (400 IU) in calcium-replete postmenopausal women reduced bone loss at the spine by 0.7%. In a follow-up report, 2 years of supplementation with 700 IU of vitamin D in healthy elderly women significantly slowed bone loss at the femoral neck, whereas supplementation with 100 IU had no effect (35). There was no significant loss at the spine in either of the supplemented groups. In contrast to the earlier report, Dawson-Hughes et al. (34) found that the combined administration of 700 IU of vitamin D and 500 mg/day calcium for 1 year significantly prevented bone loss at the spine and whole body in postmenopausal women but only at the whole body after 3 years. There was no effect on femoral neck BMD. Men, on the other hand, had a significant slowing of bone loss at all sites after 3 years of supplementation. The incidence of new fractures in both men and women was significantly reduced in the vitamin D-calcium supplemented group.

Chapuy et al. (20, 21) supplemented older institutionalized French women (~84 years of age) with vitamin D (800 IU) and calcium (1,200 mg). After 18 months of supplementation, a significant increase in femoral neck and total proximal femur BMD was observed. Furthermore, there was less bone loss in the trochanteric region, and fracture rate decreased 43% in the hip and 32% in nonvertebral regions compared to the nonsupplemented group. Moreover, levels of PTH were significantly decreased and 25(OH)D, increased in the supplemented group, providing some basis for the higher BMD measures and lower fracture rates. Ooms et al. (111) found increased femoral neck BMD and decreased PTH in noninstitutionalized elderly Dutch women following 2 years of supplementation with 400 IU of vitamin D. In this same Dutch population group, however, vitamin D, supplementation did not alter fracture rates (91). Discrepancies in the French and Dutch reports may be related to the age and health status of the population groups and overall dietary calcium intakes. Subjects in the French study were slightly older, were institutionalized, received 1,200 mg of calcium as a supplement (overall intake of ~1,700 vs. ~860 mg/day for Dutch subjects), and were administered twice as much vitamin D (800 vs. 400 IU).

Other investigators have found that calcium and vitamin D administration lowers PTH and decreases markers of bone resorption (116, 138, 143). Sorva et al. (143) reported significantly lower PTH and higher 25(OH)D, following 40 weeks of vitamin D, (1,000 IU) and calcium (1,000 mg) supplementation. Prestwood et al. (116), in a crossover design, found that 6 weeks of administration of 1,500 mg calcium citrate and 1,000 IU vitamin D, significantly lowered N-telopeptides and free deoxypyridinoline crosslinks/creatinine in 12 healthy older women (>70 years of age). PTH decreased and 25(OH)D, increased with supplementation. The link between vitamin D–calcium supplementation and attenuation of bone resorption markers may be particularly important, since Melton et al. (103) demonstrated that fractures of the hip, spine, and forearm were associated with elevated pyridinoline crosslinks. These significant negative correlations existed even after correcting for differences in BMD. Therefore, in addition to BMD measurements, bone turnover markers may help predict future risk for osteoporosis. Further investigation is warranted before markers of bone turnover can be used as clinical indices of bone fracture.

The Food and Nutrition Board has recently determined that the AIs for vitamin D are 200 IU up to 50 years of age, 400 IU between 51 to 70 years, and 600 IU over 70 years (48). The evidence suggests that vitamin D intakes of 400–800 IU in
elderly women consuming adequate calcium (1,000–1,200 mg/day) retards bone loss at the femur, and possibly the spine, and reduce fracture rates. Supplementation with vitamin D to elicit a positive bone response requires adequate intakes of calcium and should be targeted to women at high risk for poor vitamin D status.

Physical Activity and Bone Mineral

Physical inactivity also has been identified as an important risk factor in the development of osteoporosis. According to Wolff’s law, changes in bone function lead to changes in its internal architecture and external conformation (121). This idea was supported by researchers who found rapid bone loss during periods of extended bed rest (38, 73, 84) or weightlessness (154), with recovery occurring upon reambulation (38, 73, 84). Thus, increased activity and weight bearing were hypothesized to increase bone mineralization. During the past 20 years, considerable evidence has accumulated in support of this hypothesis.

Cross-Sectional Studies

Early cross-sectional studies reported greater BMD in athletes than nonathletes, suggesting that high levels of physical activity positively influenced bone mineral (107). There is now abundant cross-sectional literature supporting these early observations. Elevated BMD has been reported in female college-aged (78, 132) and former gymnasts (79), bodybuilders (68), basketball players (131), volleyball players (131), and soccer players (2). Cross-sectional studies have also demonstrated a positive relationship between physical activity and bone mineral in premenopausal and postmenopausal women. Aloia et al. (5) found that activity counts, determined using a counter attached to the waist during a 3-day period, were positively associated with total body calcium \( r = .51 \) and lumbar spine BMD \( r = .41 \) in a small sample \( n = 24 \) of nonexercising premenopausal women. Zylstra et al. (162) found lumbar spine \( n = 123 \) and femoral neck \( n = 141 \) BMD to be positively correlated with number of hours walked per day in women 21–95 years. Orwoll et al. (113) found recent or past activity to be positively associated with lumbar spine and femoral neck BMD in a large sample \( n = 7,963 \) of nonblack women ≥65 years. The positive relationship observed between muscle strength and BMD further supported the hypothesis that physical activity enhances the mineralization of bone (107).

Although cross-sectional studies have provided evidence that physical activity benefits the skeleton, they suffer from potential subject bias. The impact of genotype on BMD is believed to be substantial.

Longitudinal Studies

A number of prospective reports have demonstrated that bone mineral increases or is maintained in women following physical activity intervention. Gleeson et al. (54) were one of the first groups to demonstrate a positive change in lumbar spine BMD of premenopausal women who participated in a physical activity program compared to controls. Several longitudinal studies have demonstrated the positive influence of physical activity on bone mineral in postmenopausal women. Krolner et al. (85) found that women 50–73 years of age increased lumbar BMD by 3.5% following 8 months of moderate physical activity two times a week, compared to a 2.7%
decrease in controls. In one of the few reports examining the role of physical activity in preserving bone mineral in the elderly, Smith et al. (139) found that chair exercises at light to mild intensities (1.5–3.0 METS) significantly ($p < .05$) increased radius BMC in women 69–95 years (2.29%, $n = 12$) compared to controls (−3.29%, $n = 17$). Although these longitudinal studies and others (3, 28, 106, 120, 130) are noteworthy and support the notion of higher bone mineral with increased physical activity, the researchers’ failure to randomize their subject pool leaves the studies subject to criticism (40, 95).

Nevertheless, more recent studies using a randomized design have confirmed the earlier findings and substantiated the optimism expressed toward physical activity and its positive impact on bone mineral in premenopausal (49, 67, 92, 142), postmenopausal (11, 12, 24, 58, 82, 105, 126, 155), and elderly women (146). Despite the newfound evidence, the magnitude of the impact of physical activity on bone mineral can be questioned. While cross-sectional research comparing athletes and nonathletes suggests that physical activity markedly impacts the skeleton, this has not been substantiated in longitudinal research. Athletes who perform movements that are believed to produce high skeletal loads and stimulate bone accretion (i.e., gymnasts and weight lifters) have BMD values as much as 36% higher than controls (78). Conversely, typical improvements in BMD in women following a resistance training program are much smaller, ranging between 0.8 and 3.0% (11, 12, 24, 49, 58, 67, 82, 92, 105, 126, 142, 155). Although the improvements are not as high as once expected, if increases in BMD due to greater physical activity accumulate over time in premenopausal women and bone loss ceases in postmenopausal women, fracture risk may be significantly reduced. A 10% increase in BMD can reduce fracture risk by one half (124). Thus, improvements in adult BMD due to increased physical activity may have a substantial impact on fracture risk.

**Exercise Prescription Considerations**

Although the literature in support of physical activity as a measure of maintaining or enhancing bone mineral is growing, more research is needed to develop specific guidelines for preventing and treating osteoporosis. Important issues that must be addressed include optimal mode of physical activity, site specificity of training, the age of participants, and the effects of physical activity combined with ERT and calcium.

**Mode**

The mode of physical activity may have a substantial impact on whether bone mineral is altered following intervention. Animal studies suggest that the osteogenic response to mechanical loading is related to the magnitude of the load applied (135) and the rate of loading (110), rather than the number of loading cycles. These findings are supported by cross-sectional reports demonstrating higher BMD in athletes involved in the high-load weight-bearing activities (i.e., gymnastics) than athletes involved in low-load non-weight-bearing activities (i.e., swimming) (147, 148) and controls (78, 147, 148). A recent longitudinal report by Taaffe et al. (147) found that college-aged gymnasts gained more lumbar spine and femoral neck BMD during 8- to 12-month training periods than runners, swimmers, and controls. While activities such as gymnastics appear to provide an optimal stimulus for bone
mineralization, practical forms of physical activity that have a positive impact on bone mineral need to be identified.

**Resistance Training.** Resistance training, because of the high load imposed on the skeleton, has been promoted as an optimal form of physical activity for enhancing bone health (149). Cross-sectional reports have clearly shown weight trainers to have significantly greater than normal BMD (68, 76, 153). These findings have been supported by longitudinal studies that found resistance training to have a positive influence on BMD in women (92, 105, 142). Using a randomized design, Snow-Harter et al. (142) found that college-aged women increased lumbar spine BMD following 8 months of weight training (1.2%). In premenopausal women 28–39 years of age, Lohman et al. (92) found 5 months of weight training to positively influence lumbar spine BMD compared to controls (2.8%). Hip BMD responded at a slower rate than the more highly trabecular lumbar spine, with increases in trochanter BMD observed at 12 and 18 months (1.8 and 2.0%, respectively). Increases in bone mineralization following resistance training have also been reported in postmenopausal women (105). Using a randomized design, Nelson et al. (105) found significant increases in lumbar spine, femoral neck (Figure 5), and Ward’s triangle BMD in postmenopausal women who weight trained for 1 year versus controls.

Kerr et al. (77) tested the theory that the magnitude of the load rather than the number of loading cycles would elicit optimal changes in bone. Postmenopausal women were randomly assigned to high-load or low-load ipsilateral training programs. High-load subjects performed 3 sets of 8 repetitions at 60% of 1 repetition maximum (RM) for the lower body and 40% 1 RM for the upper body, whereas low-load subjects performed 3 sets of 20 repetitions at 20% 1 RM for the lower body and 10% 1 RM for the upper body. Despite similar increases in muscle strength, the

![Figure 5](image_url)  
**Figure 5** — Percentage change in BMD in resistance trainers (□) and controls (■) following a 1-year intervention. Values are means ± SE. Significant difference between groups, *p = .02 and **p = .04. Modified from M.E. Nelson et al. Effect of high-intensity strength training on multiple risk factors for osteoporotic fractures. *Journal of the American Medical Association* 272:1909-1914, 1994. Copyright 1994 American Medical Association.
high-load group demonstrated significant increases in trochanter, intertrochanter, Ward’s triangle, and ultradistal radius BMD, whereas the low-load group demonstrated significant BMD increases only at the midradius. These findings were supported by Taaffe et al. (146), who found that 1 year of resistance training at a high intensity (7 repetitions/set at 80% 1 RM) maintained BMD at the middle one-third of the femur (1.0 ± 1.0%) in elderly women 65–79 years old, whereas bone loss in women who trained at a low intensity (14 repetitions/set at 40% 1 RM) was similar to controls (−2.2 ± 0.5% and −1.8 ± 0.6%, respectively).

Others have demonstrated no effect or decreased BMD following resistance training programs. Rockwell et al. (133) reported decreases in lumbar spine BMD of premenopausal women who weight trained two times per week for 9 months with no change in controls. Peterson et al. (114) found no changes in lumbar spine, hip, or forearm BMD in middle-aged women following 1 year of aerobic exercise (n = 17) or aerobic exercise combined with weight training (n = 18). However, both studies suffer from methodological flaws, such as a lack of randomization of subjects and the fact that subjects in the training groups, but not controls, exercised regularly prior to the study. Moreover, the intensity of the weight training program in the Peterson study was poorly described and elicited minimal increases in strength (range = −2.6 to 14.7%).

Running and Walking. Frost (50) suggested that activities involving a large number of loading cycles, such as running and walking, are not as effective at increasing bone mineral as activities that generate high loads, such as weight training, because they do not initiate strains that surpass the “microdamage threshold range.” According to Frost, remodeling can easily repair any damage induced by strains below this range. While running and walking do not generate loads upon the skeleton equivalent to the load generated by high-load resistance training, Burr et al. (14) suggested that repetitive loads which generated ground reaction forces ≥1.5 times body mass can enhance bone formation. Furthermore, because running and walking may be more practical for some populations than activities involving high-load movements, any improvement in bone mineral brought about by these activities would warrant their use.

While running has been shown to elicit ground reaction forces of 2.5–5 times body mass at the lower limbs (145) and 1.75 times body mass at the lumbar spine (17) in humans, evidence suggesting that running increases bone mineral in premenopausal women is limited. Cross-sectional studies have found that BMD in premenopausal runners who are eumenorrheic is higher than (80, 86) or the same as (68, 69, 90, 104) controls. In one of the few longitudinal reports examining the impact of running on bone mineral in women, Snow-Harter et al. (142) found that 8 months of running increased lumbar spine BMD (1.3%) to a similar degree as weight training (1.2%) in eumenorrheic premenopausal women.

There is also a paucity of literature examining the impact of running on bone mineral in postmenopausal women. Kirk et al. (80) found that premenopausal runners, but not postmenopausal runners, tended to have higher lumbar spine BMD than age- and height-matched controls (p = .078), suggesting that older females may not benefit from running. There are no longitudinal reports examining the impact of running on bone mineral in postmenopausal women.

While running may have a positive impact on bone mineral in eumenorrheic women, the potential benefits are attenuated in women with disturbed menstrual cycles. Lumbar spine BMD has been shown to be lower in amenorrheic and
oligomenorrheic runners than eumenorrheic runners (26, 41, 104, 141) and controls (94,104). Furthermore, low lumbar spine BMD exhibited in amenorrheic runners increases significantly \((p < .01)\) upon resumption of menses (42). Taaffe et al. (147) found that training did not increase lumbar spine and femoral neck BMD in female collegiate runners, 28\% of which were suffering from oligomenorrhea or amenorrhea. Thus, a normal hormonal milieu is required for running to be beneficial to BMD.

Walking is a weight-bearing form of physical activity that is commonly prescribed to enhance physical health in women. However, whether walking helps prevent bone loss has not been established. Because walking generates lower impact forces upon the skeleton than running, it likely provides an inferior osteogenic stimulus. Nevertheless, evidence supporting the skeletal benefits of walking is more prevalent. Krall and Dawson-Hughes (83) examined the impact of current and past walking on lumbar spine and whole body BMD in healthy Caucasian women (43–72 years, \(n = 239\)) participating in a vitamin D supplementation trial. Women who walked more than 7.5 miles/week had higher whole body, leg, and trunk BMD than women who walked less than 1 mile/week. Furthermore, the number of miles walked per week during a 1-year period was positively correlated with the rate of change in leg BMD \((r = .16)\).

While, to our knowledge, there are no longitudinal reports examining the influence of walking on bone mineral in premenopausal women, a few longitudinal reports suggest that walking positively influences the skeleton in postmenopausal women (12, 58, 157). White et al. (157) (in a semirandomized study) found that postmenopausal women involved in a walking program for 6 months and matched controls lost radial BMC at a similar rate; however, significant increases in radial bone width and cross-sectional moment of inertia were found in walkers only. Brook-Wavell et al. (12) found that regular brisk walking for 1 year increased BMD significantly at the calcaneus \((p < .05)\) and almost significantly at the lumbar spine \((p < .08)\) in postmenopausal women (60–70 years, \(n = 39\)) compared to controls \((n = 40)\). Significant increases in BMD of the walkers were also observed at the femoral neck \((p < .05)\); however, the change was not significantly different from controls. Ebrahim et al. (43) found that loss of femoral neck BMD was almost significantly greater in postmenopausal women who performed upper limb exercises compared to women who walked briskly three times/week for 2 years \((-2.8\% \text{ vs. } -0.25\%, p = .056)\).

Whether walking significantly impacts bone mineral may depend upon its intensity. Using a randomized design, Hatori et al. (58) found that walking at an intensity above the anaerobic threshold \((110\% \text{ of heart rate at anaerobic threshold})\) attenuated bone loss at the lumbar spine in postmenopausal women \((n = 12)\), whereas walking at an intensity below the anaerobic threshold \((90\% \text{ of heart rate at anaerobic threshold})\) had no influence on BMD \((n = 9); \text{ Figure 6}\). The greater response to higher intensity walking was probably due to higher ground reaction forces that occur at faster walking speeds. Increasing walking speed from 1.0 m/s to 3.0 m/s has been shown to increase ground reaction forces by 50\%, from 1.0 to 1.5 times body mass (108).

Conversely, others have reported no changes in bone in postmenopausal women following a walking program. Sandler et al. (136) found that a 3-year walking program had no influence on radial bone loss in postmenopausal women. However, bone changes were not assessed at loaded sites, such as the lumbar spine and hip. Further, the intensity of the walking was not described. Cavanaugh et al. (18) found that walking at 60–85\% of age-predicted maximum heart rate for 15–40 min, three times/week for 1 year, did not attenuate lumbar spine trabecular bone loss in
postmenopausal women compared to controls. However, this study lacked randomization, and walkers exhibited a significantly higher amount of baseline weight-bearing physical activity than controls.

**Jumping and Aerobic Dance.** Other practical forms of high-load physical activity, such as jumping and aerobic dance, may provide a better stimulus for increasing bone mineral than running or walking. While Umemura et al. (151) found higher femur and tibia fat-free weight in rats who jumped from a height of 40 cm, 100 times/day, 5 days/week for 8 weeks and rats who ran for 60 min/day than sedentary rats, the bone values were highest in the jump-trained rats. Furthermore, higher bone values were demonstrated in young and old jump-trained rats, whereas only younger run-trained rats had elevated values. More recently, Umemura et al. (152) found that 5-week-old rats who jumped from a 40 cm height just 5 times/day, 5 days/week for 8 weeks, had higher femur and tibia fat-free weight than control rats. Human data also support jumping as an osteogenic form of physical activity. An 18-month randomized trial by Heinonen et al. (67) found that premenopausal women involved in high-load physical activity (jump training) that elicited ground reaction forces 2.1 to 5.6 times body mass increased lumbar spine, femoral neck, distal femur, patella, proximal tibia and calcaneus BMD compared to controls. Moreover, Bassey and Ramsdale (9) found significant increases in trochanter BMD of premenopausal women following a 6-month training program that included jumping, with no changes observed in controls.

The bones of postmenopausal women may also be responsive to high-load aerobic dance and jumping. White et al. (157) found that 6 months of aerobic dance maintained radial BMC in postmenopausal women, whereas significant losses were found in walkers and controls. In a partly randomized study, Welsh and Rutherford (155) found that 1 year of aerobic activity including high-load step and jumping
exercises significantly increased femoral neck and trochanter BMD in a group of previously sedentary men \((n = 6)\) and postmenopausal women \((n = 9)\), whereas no changes were exhibited in matched controls \((n = 15)\).

**Ground Reaction Forces Versus Joint Reaction Forces.** While the magnitude of the loads applied to the skeleton appears to be an important regulator of bone mineralization, the nature in which the stress is applied may also influence its impact on bone. Kohrt et al. \((81)\) found that activities which stressed the skeleton through ground reaction forces, such as walking, jogging, and stairclimbing, or through joint reaction forces, such as weight training and rowing, significantly increased lumbar spine, Ward’s triangle, and whole body BMD in older women \((60-74\) years), whereas only activities that created significant ground reaction forces increased femoral neck BMD \((3.5 \pm 0.8\% \text{ vs. } -0.2 \pm 0.7\%)\). The authors suggested that ground reaction forces may provide a better osteogenic stimulus at the femoral neck than activities that stress the skeleton through joint reaction forces. In contrast, Nelson et al. \((105)\) found that weight training, an activity which creates joint reaction forces, significantly increased femoral neck BMD in postmenopausal women compared to controls. Furthermore, Bassey et al. \((10)\) found that performing “heel drops,” which cause ground reaction forces between 2.5 and 3 times body mass, 50 times each day had no impact on lumbar spine or proximal femur BMD in postmenopausal women compared to subjects who performed flexibility and low-impact exercise.

In summary, high-load physical activities, such as resistance training and jumping, appear to provide the best stimulus for enhancing BMD in premenopausal and postmenopausal women. Lower load activities, such as running and high-intensity walking, may also benefit BMD, but further investigation is needed. It is unclear whether activities that create ground reaction forces, joint reaction forces, or both provide the greatest osteogenic stimulus to the skeleton.

**Specificity of Training**

The benefits of physical activity on BMD are believed to be site specific. This concept is supported by cross-sectional reports demonstrating higher indices of bone mineral in the playing versus nonplaying arm of athletes involved in racquet sports \((72, 115)\), and longitudinal reports finding augmented bone mineral at physically trained sites but not at untrained sites. Using a randomized design, Revel et al. \((126)\) found that 34 postmenopausal women who performed psoas muscle exercises \((60\) hip flexions with each leg while seated) each day with a 5-\(kg\) weight on the knee, for 1 year, tended \((p < .09)\) to lose less lumbar spine trabecular BMD than \(33\) controls who performed deltoid exercises \((-0.57 \pm 1.36 \text{ mg/cm}^3 \text{ vs. } -7.05 \pm 12.55 \text{ mg/cm}^3)\). When the groups were subdivided to include only those subjects who performed their exercises at least \(5\) times/week, lumbar spine trabecular BMD in the psoas group \((n = 23)\) did not change \((0.14 \pm 11.21 \text{ mg/cm}^3)\), whereas it decreased in the deltoid group \((-8.87 \pm 12.75 \text{ mg/cm}^3, p = 0.01, n = 26)\). Since the psoas muscles, but not the deltoid muscles, attach at the lumbar spine and participate in hip flexion, these data suggest that the pulling forces generated by muscles at their attachments on bone may be one mechanism that activates the mineralization process. Mayoux-Benhamou et al. \((99)\) followed the group for an additional \(2\) years and found that the psoas group \((n = 21)\) lost significantly \((p = .02)\) less lumbar spine BMD than the deltoid group \((n = 14)\) during the \(3\)-year period \((-9.26 \pm 28.45 \text{ mg/cm}^3 \text{ vs. } -16.79 \pm 8.51 \text{ mg/cm}^3)\).
Kerr et al. (77) found that intense strength training designed to stress the proximal femur (i.e., hip extension, flexion, abduction and adduction, and leg press) and the forearm (i.e., wrist curls, pronation, and supination, and biceps curl) significantly increased trochanter, intertrochanter, and Ward’s triangle BMD in the exercising leg \((n = 23)\) and ulnar distal radius BMD in the exercising forearm \((n = 25)\) of postmenopausal women. Since the psoas and iliacus muscles attach at the lesser trochanter and the lesser trochanter is included in the intertrochanteric site, the authors hypothesized that the increases in intertrochanteric BMD were due, in part, to the pulling of the psoas and iliacus muscles during hip flexion. This hypothesis was supported by a positive correlation between the change in hip flexion strength and the change in trochanteric BMD \((r = .60, p < .01)\). No changes were found in the nonexercising limbs. A similar connection was made at the greater trochanter. The gluteus maximus, which inserts at the greater trochanter, is primarily responsible for hip extension. A positive correlation was observed between the change in hip extension strength and the change in BMD at the trochanter \((r = .51, p < .01)\).

In summary, changes in BMD occur at specific sites within the skeleton by exercising their attaching muscles. Consequently, activities that involve hip flexion and extension may be necessary to enhance BMD at the lumbar spine and hip.

**Age of Participants**

It has been suggested that the response to physical activity may be different in premenopausal, early and late postmenopausal, and elderly \((\geq 75\) years) women. Bone in the young adult skeleton is believed to be more responsive to physical stimuli than bone in the older adult. Rubin et al. (134) found that the ulna of young adult turkeys \((\sim 1\) year old) subjected to 300 cycles of a high but physiological level of normal strain increased in cross-sectional area \((30.2 \pm 7.8\%)\), whereas the ulna of older turkeys \((\sim 3\) years) remained unchanged \((-3.3 \pm 7.5\%)\). The authors suggested that the lack of response in the older skeleton may be due to deterioration in the ability of the bone cell to detect osteogenic signals or inability to respond to the signals.

Experimental research conducted on rats with intact ovaries suggests that increases in bone mineral in premenopausal women following increased physical activity are due to increased bone formation (161). These reports are supported by the work of Lohman et al. (92), who found increases in BMD accompanied by increases in osteocalcin, a measure of bone formation, in premenopausal women following an 18-month resistance training program. Conversely, data on ovariectomized rats suggest that increases in bone mineral in postmenopausal women following increased physical activity may be due to decreased resorption (159, 160). These data are supported by Welsh and Rutherford (155), who observed decreases in pyridinoline \((-19.0 \pm 7.2\%)\) and deoxypyridinoline \((-20.0 \pm 7.7\%)\) cross-links in men and postmenopausal women following a 6-month physical activity program.

Hatori et al. (58) found no changes in the urinary hydroxyproline-to-creatinine ratio, a marker of bone resorption, in postmenopausal women following 7-months of high-intensity or low-intensity walking. However, increases in the urinary hydroxyproline-to-creatinine ratio were observed in controls, suggesting that increased physical activity minimizes increases in bone resorption typically found in postmenopausal women. It is unclear whether bone formation is altered with increased physical activity in postmenopausal women, since increased (105), decreased (28), and unchanged (58, 81) osteocalcin levels have been reported.
The number of years past the onset of menopause may also alter the impact of physical activity on bone mineral. Martin and Notelevitz (96) found treadmill training for 1 year to have no impact on lumbar spine and forearm BMD in a sample of postmenopausal women, but when subjects were divided based on years past menopause, aerobic physical activity was found to attenuate bone loss in those who were ≤6 years past the onset of menopause. Others have reported positive changes in BMD following increased physical activity in women ≤6 years (120) and >6 years (11, 12, 81, 105) past menopause.

Burckhardt (13) suggested that exercises which may attenuate bone loss in women <75 years are probably impractical for women >75 years. Thus, recommendations need to be developed that are specific to the elderly population. Spending more time on one’s feet may be one measure of reducing bone loss. Based on bed rest data, Issekutz et al. (73) suggested that the minimum amount of time exposed to the stress of gravity in the upright position required to prevent bone loss is approximately 3 hr/day. They concluded that the increase in urinary calcium output while in a prolonged horizontal position was due to the absence of longitudinal pressure (weight bearing) on the bones rather than physical inactivity. This is supported by Cummings et al. (27), who found that spending less than 4 hr/day on the feet was one of the five most important risk factors for hip fracture.

While longitudinal data supporting a positive impact of physical activity on bone mineral in elderly women are scarce, the little available data are promising (146). Moreover, Cummings et al. (27) followed Caucasian women (N = 9,516) ≥65 years for 4.1 years and found walking to decrease the risk of hip fracture. The reduction in fracture risk may be due, in part, to a reduction in the number of falls. Using a meta-analysis, Province et al. (119) found exercise intervention to reduce falling frequency by 10% in the elderly. However, activities that are specifically designed to increase muscular strength, endurance, and balance may be necessary to decrease falling frequency. Ebrahim et al. (43) found that women involved in a walking program had a significantly (p < .05) higher incidence of falls than controls during a 2-year period, whereas Campbell et al. (16) found that elderly women (≥80 years) who participated in a 1-year program that included strength and balance exercises in addition to walking had a significantly lower number of falls than controls (88 vs. 152 falls). More studies involving the elderly are needed to identify specific physical activities that reduce skeletal fractures, especially at critical sites such as the proximal femur and lumbar spine.

Physical Activity, Estrogen Replacement Therapy, and Calcium

While physical activity, calcium supplementation, and ERT independently can have a positive influence on bone mineral in postmenopausal women, their combined effects may be even greater. Notelevitz et al. (109) found that resistance training combined with ERT in surgically postmenopausal women (n = 9) significantly increased whole body, lumbar spine, and radial BMD and BMC (2.1–8.3%), whereas no significant change was reported using ERT alone (n = 11); unfortunately, the study lacked a control group. Heikkinen et al. (66), using a randomized design, found that performing loading exercises for the lumbar spine and femur 3 hr/week for 2 years significantly increased femoral neck BMD but not lumbar spine BMD in early postmenopausal women (49–55 years, 0.5–3 years past the onset of menopause). Estrogen replacement therapy alone significantly increased femoral
neck, Ward’s triangle, and trochanter BMD (p < .05); however, changes in BMD were not further improved when ERT was combined with physical activity.

A different response to physical activity combined with ERT may be found in women who are later in the postmenopausal period. Prince et al. (118) found that physical activity (one weekly exercise class and two 30-min brisk walks per week) combined with ERT for 2 years significantly increased distal and medial forearm BMD in women ~5.5 years past menopause, compared with physical activity alone and controls. Kohrt et al. (82), studying postmenopausal women greater than 10 years past menopause, found a 9-month, weight-bearing physical activity program to increase lumbar spine, femoral neck, trochanter, and Ward’s triangle BMD similar to those from ERT (60–72 years). However, when physical activity and ERT were combined, increases in lumbar spine and whole body BMD were greater than either treatment alone (p < .01) and were close to being significantly greater at Ward’s triangle (p = .08).

While ERT may be a more effective adjunct to physical activity than calcium in enhancing bone mineral of postmenopausal women, Prince et al. (118) found that calcium supplementation (~1,000 mg) could provide some additional benefit. Furthermore, Prince et al. (117) found that supplementing calcium intake from ~800 to 1,800 mg/day with calcium tablets or milk powder significantly reduced bone loss at the intertrochanteric and trochanteric hip in women ≥10 years past menopause. When calcium supplementation was combined with physical activity, a significant reduction was also found at the femoral neck. Based on a meta-analysis of 17 intervention trials, Specker (144) concluded that a moderately high calcium intake (≤1,000 mg/day) may be necessary to reap the benefits of physical activity on bone.

Thus, the effect of physical activity and ERT on bone mineral may be additive in women >5 years past menopause. Limited data suggest that moderately high levels of calcium can accentuate bone gain associated with increased physical activity in postmenopausal women; however, research examining their combined impact on bone mineral in premenopausal women is needed.

**Summary**

The relationship between calcium intake and bone mineral is weakly supported in cross-sectional and observational studies; however, randomized, double-blind, placebo-controlled intervention studies support calcium supplementation for the maintenance and prevention of bone loss in premenopausal and late postmenopausal women. In premenopausal women, the protective effect of supplementation has been reported at the whole body, humerus, and lumbar spine with approximately 1,000–1,500 mg of calcium. In the early postmenopausal years, calcium supplementation has modest effects (less than 1%) on primarily cortical bone sites including the proximal forearm, distal radius, and metacarpal bone. While calcium supplementation does not replace ERT, it should be used as an adjunct if dietary calcium intakes are low. Calcium supplementation is capable of slowing bone loss at cortical bone sites such as the humerus, radius, and femur in late postmenopausal women consuming calcium at levels lower than recommended by NIH. A reduction in fracture incidence following calcium supplementation has also been reported in postmenopausal women, potentially the result of reduced bone turnover and the suppression of high PTH levels. Phytoestrogens fed in large amounts to rats have
demonstrated the potential for slowing bone loss in ovariectomized rats; however, these data need to be confirmed in humans.

The elderly are at risk for poor vitamin D status because of low intakes, reduced UV exposure, and decreased synthesis of the active form of vitamin D. Supplementing elderly women with 400–800 IU of vitamin D₃ combined with additional calcium slows bone loss at the spine and femoral neck and reduces fracture rates. Not only women who are frail or institutionalized, a group that increasingly makes up a large segment of the world population, but also healthy older women may benefit from vitamin D supplementation.

Physical inactivity can reduce bone mineral and lead to fractures related to osteoporosis. Activities that include high-load movements appear to provide the greatest stimulus for enhancing bone mineral. Cross-sectional studies have clearly demonstrated that athletes who regularly perform high-load movements tend to have higher BMD than athletes in general and the average population. Although early longitudinal reports were criticized for lacking randomization, more recent reports using a randomized design have demonstrated that physical activity, especially that which is weight bearing and loads the skeleton to a greater extent than normal activities of living, can improve BMD in premenopausal and postmenopausal women. The large discrepancy that has been demonstrated between athletes and nonathletes in cross-sectional studies is much greater than changes typically observed following an intervention study; however, if small improvements in BMD accumulate over time, a substantial improvement in fracture risk may result. Furthermore, increased physical activity, especially activities designed to increase muscular strength, endurance, and balance, may reduce fracture risk by decreasing the incidence of falling.

The benefits of physical activity on bone mineral appear to be even more pronounced when combined with ERT in late postmenopausal women. Although calcium may not complement the bone-enhancing properties of physical activity as well as ERT, limited data suggest that it may provide some benefit. More research is needed to confirm the impact of physical activity combined with ERT and calcium. While current research suggests a positive impact of physical activity on skeletal mineralization, whether improved bone mineral can be augmented in premenopausal women and maintained in postmenopausal women requires investigation over periods greater than 2 years. Consequently, additional research is needed to develop specific and practical physical activity guidelines to aid in the prevention and treatment of osteoporosis.

References


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