



Clinical Practice Guideline for the Prevention, Diagnosis and Treatment of Osteoporosis

Osteoporosis is a disease characterized by low bone mass and loss of bone tissue that may lead to weak and fragile bones. If you have osteoporosis, you have an increased risk for fractured bones, particularly in the hip, spine, and wrist. Osteoporosis is often considered to be a condition that frail elderly women develop. However, the damage from osteoporosis begins much earlier in life. Because peak bone density is reached at approximately 25 years of age, it is important to build strong bones by that age, so that the bones will remain strong later in life. Adequate calcium intake is an essential part of building strong bones.

In the United States, nearly 10 million people already have osteoporosis. Another 18 million people have low bone mass that places them at an increased risk for developing osteoporosis. As our population ages, these numbers will increase. About 80% of those with osteoporosis are women. Of people older than 50 years of age, one in two women and one in eight men are predicted to have an osteoporosis-related fracture in their lifetime. According to the World Health Organization, the prevalence of osteoporosis among U.S. white women past menopause is estimated to be 14% in those 50-59 years of age, 22% in those 60-69 years of age, 39% in those 70-79 years of age, and 70% in those 80 years of age and older. Significant risk has been reported in people of all ethnic backgrounds. White and Asian racial groups, however, are at greatest risk.

Primary Prevention of Fracture

Body Habitus: Low BMI (less than 20) is a strong independent risk factor for osteoporosis and fracture. Weight less than 127 pounds, associated with small bones, is a risk factor for osteoporosis. Primary prevention should include counseling patients on achievement and maintenance of a healthy body weight (BMI between 20 and 25). A balanced diet including dairy products and appropriate nutrition should be discussed with patients.

Gonadal Hormone Status: Women who are prematurely hypogonadal and hypogonadal men who are at increased risk for fracture should be considered for replacement therapy.

Exercise: Exercise is well known for its many benefits both short-term and long-term. Weight bearing and muscle strengthening exercises have been shown to be an integral part of osteoporosis prevention as well as a part of the treatment process. Three components of an exercise program are needed for strong bone health: impact exercise such as jogging, brisk walking, stair climbing; strengthening exercise with weights; and balance training such as Tai Chi or dancing.

Smoking Cessation: Smoking cessation counseling should be done at every visit. Discussion can include helpful strategies such as nicotine replacement therapy with patches, gum, etc. Bupropion, varenicline, and available smoking cessation classes may also be discussed.

Alcohol Restriction: Limit alcohol use to no more than two drinks per day. One drink equals 12 ounces of beer, 5 ounces of wine, or 1.5 ounces of 80-proof distilled spirits. This limit will help to protect bone health and reduce the risk of falls.

Calcium: Adequate calcium intake from food sources and supplements promotes bone health. When food sources do not provide enough calcium, supplements can be used to meet this goal. Bioavailability of calcium in food sources and supplements is a factor in achieving daily calcium recommendations. See United States Department of Agriculture (USDA) table for foods rich in calcium (<http://www.nal.usda.gov/fnic/foodcomp/search>).

Daily elemental calcium recommendations for healthy individuals from diet and supplement include:

- 19-50 years: 1,000 mg
- Over 50 years: 1,200 mg
- Maximum limit: 2,150 mg

However, for people with established osteoporosis, glucocorticoid therapy, pregnant or nursing women, or persons over the age of 65, it may be more appropriate to recommend 1,500 mg.

Calcium supplementation has been shown to increase the ratio of high-density lipoprotein (HDL) cholesterol to low-density lipoprotein (LDL) cholesterol by almost 20% in healthy postmenopausal women by binding to fatty acids in the gut. Over-supplementation, however, has not been shown to translate into reduced coronary or cerebrovascular events, particularly in the elderly who may have compromised kidney function. Over-supplementation may be associated with an increased risk of kidney stones and vascular calcification.

Both low fractional calcium absorption and low dietary calcium intake have been associated with increased fracture risk. Since fractional calcium absorption is affected by multiple factors and decreases with age, adequate lifetime dietary calcium is an important recommendation for bone health.

Calcium absorption is compromised when oxalic acid is present in foods such as dark, green, leafy vegetables. An exception is soybeans. A variety of foods with calcium is recommended.

Bioavailability from calcium supplements is affected by meals, dose size and tablet disintegration. Calcium absorption decreases at doses greater than 600 mg; therefore, supplements should be taken with meals and in divided doses. Taking calcium carbonate supplements on an empty stomach may increase the risk of kidney stones. Heavy metal levels in calcium supplements vary, with some supplements exceeding the acceptable level, and absorption of calcium carbonate may be decreased in the environment of high-dose proton-pump inhibitor use or histamine receptor blockers.

Vitamin D: Adequate vitamin D intake supports calcium absorption and bone metabolism. Since sunlight exposure cannot be assumed to produce needed vitamin D, dietary sources are essential. Many adults are deficient in vitamin D, and supplements are often needed to meet daily requirements.

Recent studies concerning vitamin D and bone health demonstrate daily vitamin D supplementation in the range of 700-800 international units can decrease hip fracture risk in the elderly by 26% and any non-vertebral fracture by 23%.

The effects of optimal vitamin D levels include:

- Maximum suppression of circulating parathyroid hormone (PTH)
- Increased calcium absorption
- Decreased rates of bone loss
- Decreased risk of falling (22%)
- Improved lower extremity functioning

The high-risk group (i.e., the elderly, long-term care residents and those with no sunlight exposure) would be expected to receive the greatest benefit from vitamin D supplementation.

Target levels for optimum 25-OH vitamin D are 30 ng/mL or 80 nmol/L and often require oral supplementation of 700-1,000 international units. However, most multivitamins contain 400 international units vitamin D, which may be inadequate.

Vitamin D₂ (ergocalciferol) is equally effective as vitamin D₃ (cholecalciferol) in maintaining 25-OH vitamin D serum levels when given at 1,000 international units daily

Prevention of Falls: Preventing falls reduces fracture risk. Modifying environmental, personal risk, and medication-related factors can be effective in reducing falls. Home visits may help with this. In addition to vitamin D supplementation, hip protector pads for frail, elderly adults have been shown to reduce hip fractures in some studies, but not in others. Measures to decrease kyphotic posture and improve unsteady gait such as Tai Chi can decrease falls.

Risk Factors

The following are risk factors for osteoporosis and osteoporotic fracture:

- Prior fragility fracture
- Parental history of hip fracture
- Current tobacco smoker
- Long-term use of oral glucocorticoids
- Rheumatoid Arthritis
- Secondary causes of osteoporosis
- Daily alcohol use (3 or more units)
- Advanced age (> 65)
- Body Habitus (weight < 127 lbs, BMI \leq 20)
- Caucasian or Asian race
- Hypogonadism
- Sedentary Lifestyle
- Diet deficient in calcium or Vitamin D without adequate supplementation
- Increased likelihood of falling

Bone Density Assessment

BMD measurement with DXA is the single best imaging predictor of fracture risk as well as the best monitor of patient response to treatment. DXA is ideally performed by a technologist certified by the International Society of Clinical Densitometry (ISCD) or the American Registry of Radiologic Technologists (ARRT).

Measurements of BMD with DXA can predict fracture risk and allow for the identification of people who are at increased risk of fracture. Reviews of prospective cohort studies and case control studies have documented a direct relationship between decreasing BMD and increasing bone fracture risk. Additionally, there is strong evidence that stabilization or increases in BMD with therapy for osteoporosis are associated with substantial reductions in fracture incidence. Therefore, densitometry offers an objective measurement of a patient's response to treatment over time $[M]$, $[R]$. At this time there are not cost effectiveness data for monitoring response to treatment. Current practice is to describe an individual's bone mineral density as compared to a reference normal population. In this sense, a T-score is the number of standard deviations above or below the mean for a gender- and ethnicity-matched young adult healthy population.

Normal, low bone density (osteopenia) and osteoporosis are defined by the lowest of lumbar spine (at least two evaluable vertebrae required), femoral neck, and total femur T-score, according to the World Health Organization (WHO). The one-third radius site may be used if either the lumbar spine or femur is non-evaluable. Although the following classifications were originally drafted for Caucasian postmenopausal women, this also applies to men age 65 and older.

- Normal: A T-score greater than or equal to -1
- Low bone density (osteopenia): A T-score between -1 and -2.5
- Osteoporosis: A T-score less than or equal to -2.5
- The term "severe osteoporosis" is reserved for patients with a fragility fracture(s) *and* a low bone density

The National Osteoporosis Foundation recommends bone density testing in the following:

- Women age 65 and older and men age 70 and older, regardless of clinical risk factors

- Younger postmenopausal women and men age 50-70 about whom you have concern based on their clinical risk factor profile
- Women in the menopausal transition if there is a specific risk factor associated with increased fracture risk such as low body weight, prior low-trauma fracture, or high-risk medication
- Adults who have a fracture after age 50
- Adults with a condition (e.g., rheumatoid arthritis) or taking a medication (e.g., glucocorticoids greater than or equal to 5 mg/day for three months or longer) associated with low bone mass or bone loss
- Anyone being considered for pharmacologic therapy for osteoporosis
- Anyone not receiving therapy in whom evidence of bone loss would lead to treatment
- Postmenopausal women discontinuing estrogen should be considered for bone density testing

Treatment

Gonadal Hormone Treatment: The use of supplemental estrogen in the immediate postmenopause has been well accepted in preventing the rapid loss of bone that occurs in this interval. Ultra-low estrogen supplementation has been shown to be effective in severely hypoestrogenic women in improving bone mass (Female). The bone loss associated with male hypogonadism is reversed by testosterone therapy at least partly via aromatization to estrogen. Testosterone therapy, although not FDA-approved for osteoporosis, seems a reasonable first therapeutic intervention in men symptomatic with hypogonadism who do not have contraindications to the use of testosterone therapy (Male).

Bisphosphonates: Alendronate has been shown to increase bone mineral density and reduce the incidence of vertebral, hip, and non-vertebral fractures in postmenopausal women having existing vertebral fractures, and those with low bone mineral density (approximately 2.1 SD below peak) compared to placebo (calcium and vitamin D). Excellent clinical trial data based on BMD and bio-markers supports the use of oral bisphosphonates for preventing fractures in patients diagnosed with postmenopausal low bone density (osteopenia) or osteoporosis. The best clinical trials have been done with alendronate, risedronate, and ibandronate.

Selective Estrogen Receptor Modulator (SERM): The only SERM approved for the prevention and treatment of osteoporosis is raloxifene. The MORE trial was a large 3-year randomized placebo-controlled study in postmenopausal women with osteoporosis. Raloxifene showed an increase in BMD and reduced the risk of vertebral fractures. The risk of non-vertebral fractures did not differ between placebo and raloxifene. There was an increased risk of venous thromboembolism compared with placebo (RR 3.1, 95% CI 1.5-6.2). The CORE 4-year trial extension of 4,011 women continuing from MORE (7,705) showed no difference in overall mortality, cardiovascular events, cancer or nonvertebral fracture rates. In the STAR trial, raloxifene was found comparable to tamoxifen for the prevention of invasive breast cancer. Thus, raloxifene appears to be the drug of choice for women with osteoporosis if the main risk is of spinal fracture and there is an elevated risk of breast cancer.

Calcitonin: Nasal salmon-calcitonin 200 international units daily has shown a 33% risk reduction in new vertebral fractures compared with placebo (RR 0.67, 95% CI 0.47-0.97, $p = 0.03$). This occurred without significant effects on BMD. BMD measurements were not blinded to investigators and 59% (744) participants withdrew from the study early. Also, a dose response was not observed with respect to risk reduction of vertebral fractures.

Follow-Up after Pharmacologic Intervention

Periodic follow-up central DXA on the same machine is recommended for following patients on pharmacologic therapy. The testing interval varies from 6 to 24 months depending on the clinical situations. Sequential bone density testing using central DXA may be useful, and is generally recommended in monitoring drug therapy for the treatment of osteopenia or osteoporosis. Ideally, such testing should be performed on the same machine as the pre-treatment bone density and no more than every 12 to 24 months. A frequency as often as every 6 to 12 months may be indicated in the case of glucocorticoid treated patients or those on suppressive doses of thyroid hormone. Other patients at risk for accelerated bone loss include women at early menopause or those who have discontinued estrogen and are not on another bone protective agent*. The lumbar spine and the total proximal femur have the highest reproducibility and are the preferred sites for monitoring therapy. Changes in BMD should only be reported as significant if they exceed the "least significant

change" for the DXA center. Stability or increase in BMD indicates successful therapy. A significant decline in BMD may require further investigation.

A significant decrease in BMD on therapy may be due to:

- Poor drug adherence
- Improper medication administration technique in the case of bisphosphonates
- A missed secondary cause of osteoporosis (e.g., hyperparathyroidism, malabsorption)
- Inadequate calcium intake
- Untreated Vitamin D deficiency
- A true treatment failure due to the drug itself
- Malabsorption of orally administered drugs

References

Diagnosis and Treatment of Osteoporosis. Institute for Clinical Systems Improvement (ICSI). September, 2008. Accessed via the National Guideline Clearinghouse (NGC).

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