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Management of Osteoporosis

Clinical Practice Guideline
Effective August 2007
(Revised 10/09)

This guideline is based upon the Management of Osteoporosis guideline developed by an expert committee of the National Osteoporosis Foundation (NOF) in collaboration with a multi-specialty council of medical experts in the field of bone health convened by the NOF and originally published in 1999 and most recently updated in 2008. In some cases, whole sections and tables of the NOF Guideline have been incorporated into this guideline without any modifications. It is designed to serve as a basic reference on the prevention, diagnosis, and treatment of osteoporosis for postmenopausal women and men above the age of 50. Prevention recommendations can be universally applied. It is intended for use by physicians as a tool for clinical decision making in the treatment of individual patients.

Overview

Osteoporosis is a silent disease process that takes an enormous medical and economic toll on an aging population. Although osteoporosis is generally preventable and treatable, its first clinical manifestation is usually a fracture, sometimes a major and disabling one. Prevention, detection, and treatment of osteoporosis should be a mandate of primary care, particularly patients at highest risk. Based on an analysis of current research by experts convened by the National Osteoporosis Foundation, this guide offers concise recommendations regarding prevention, risk assessment, diagnosis (including indications for, and interpretation of, bone mineral density testing), and treatment, including diet, exercise, and pharmacologic treatment where indicated for postmenopausal female patients and men 50 years of age and older.

Scope of the Problem

According to the NOF Guideline, osteoporosis affects an enormous number of people, of both sexes and all races, and its prevalence will increase as the population ages. Based on data from the National Health and Nutrition Examination Survey III (NHANES III), NOF has estimated that more than 10 million Americans have osteoporosis and an additional 33.6 million have low bone density of the hip. One out of every two white women will experience an osteoporotic fracture at some point in her lifetime. One in five men will have an osteoporosis related fracture in his lifetime. Osteoporosis is less common in African American women represents the same risk of fracture once it occurs.

Major Recommendations

Recommendations apply to postmenopausal women and men age 50 and older.

1. Counsel patients on the risk factors for osteoporosis. Osteoporosis is a “silent” risk factor for fracture just as hypertension is for stroke
2. Perform evaluation for osteoporosis on all postmenopausal women who present with fractures, using bone mineral density (BMD) testing to confirm the diagnosis and determine disease severity.
3. Recommend BMD testing to postmenopausal women under age 65 who have one or more additional risk factors for osteoporotic fracture (Low body wt., <57.6 kg. or Family Hx of. Fracture hips or spine).
4. In postmenopausal women and men age 50-69, recommend BMD testing when you have concern based on their risk factor profile.

5. Recommend BMD testing to all women aged 65 and older and men age 70 and older regardless of additional risk factors.
6. According to National Osteoporosis Foundation (NOF) recommendations, adults under age 50 need 1,000 mg of calcium daily, and adults age 50 and over need 1,200 mg of calcium daily. If patients have difficulty getting enough calcium from the foods they eat they should take a calcium supplement to make up the difference. Vitamin D is necessary for optimal absorption of calcium, the NOF recommends 400 to 800 IU per day Vitamin D_3 for individuals under the age of 50, and 800-1000 IU of Vitamin D_3 for adults age 50 older. Vitamin D_3 is the form of vitamin D that best supports bone health.
7. Recommend regular weight-bearing and muscle-strengthening exercise to reduce the risk of falls and fractures.
8. Advise patients to avoid tobacco smoking and to keep alcohol intake moderate.
9. Initiate treatment in those with hip or vertebral (clinical or morphometric) fractures.
10. Initiate therapy in those with BMD T-scores ≤ -2.5 at the femoral neck or spine by dual-energy x-ray absorptiometry (DXA), after appropriate evaluation.
11. Initiate treatment in postmenopausal women and men age 50 and older with low bone mass (T-score between -1.0 and -2.5, osteopenia) at the femoral neck or spine and a 10-year hip fracture probability ≥ 3% or a 10-year major osteoporosis related fracture probability ≥ 20% based on the US-adapted WHO absolutefracture risk model (FRAX™; www.NOF.org and www.shef.ac.uk/FRAX).
12. Current FDA-approved pharmacologic options for osteoporosis prevention and/or treatment are bisphosphonates (alendronate, ibandronate, risedronate and zoledronic acid), calcitonin, estrogens and/or hormone therapy, parathyroid hormone (teriparatide) and estrogen agonist/antagonist (raloxifene).
13. BMD testing performed in DXA centers using accepted quality assurance measures is appropriate for monitoring bone loss. For patients on pharmacotherapy, it is typically performed two years after initiating therapy and every two years thereafter; however, more frequent testing may be warranted in certain clinical situations.

Risk Factors for Osteoporotic Fracture

The factors associated with an increased risk of osteoporotic fracture can be characterized as modifiable or nonmodifiable. In general, the more risk factors a patient has, the greater the risk of fracture. If one or more risk factors are present, bone mineral density (BMD) testing may be indicated to determine whether therapy is appropriate.

Non-Modifiable	**Potentially Modifiable**
▪ **Personal history of fracture as an adult**	▪ **Current cigarette smoking**
▪ **History of fracture in first-degree relative**	▪ Early menopause or bilateral oophrectomy
▪ Female sex	▪ Prolonged premenopausal amenorrhea
	▪ (>1 year)
▪ Poor health/ frailty	▪ Alcohol (3 or more drinks/day)
▪ Caucasian race	▪ **Low body weight (<127 lbs)**
▪ Advanced age	▪ High intake Aluminum containing antacids
▪ Dementia	▪ Excess Vitamin A intake
	▪ Vitamin D insufficiency
	▪ High salt or caffeine intake
	▪ Low calcium intake (lifelong)
	▪ Impaired eyesight despite adequate correction
	▪ Poor health/frailty
	▪ Recurrent falls
	▪ Inadequate physical activity/Immobilization

1. Note that poor health and frailty, which may or may not be modifiable, appear under both headings.
2. **The four items in boldface—personal or family history of fracture, smoking, and low body weight—were demonstrated in a large, ongoing, prospective US Study to be key factors in determining the risk of hip fracture (independent of bone density).**

Falls and the risk of a fall are an important part of the evaluation since the majority of osteoporosis-related fractures result from falls. The most important of these seem to be a personal history of falling, along with muscle weakness and gait, balance and visual deficits.11

Environmental issues of concern which can often be modified to reduce risk include: lack of assistive devices in bathrooms, loose throw rugs, low level lighting, obstacles in the walking path, and slippery outdoor conditions

Medical conditions may also increase the risk of fall. They include: previous fall, age, anxiety, arrhythmias, dehydration/orthostatic hypotension, female gender, impaired transfer and mobility, reduced proprioception, muscle weakness, malnutrition, diminished mental acuity/cognitive functioning, urgent urinary incontinence, medications that cause sedation, kyphosis, and poor vision.

A recent study (Kannus & Parkkari, 2007, p. 454) suggested that in nursing home and institutions with high rates of hip fracture the use of hip protectors might help to reduce the risk of fracture. “However there is no evidence to benefit from hip protectors for lower-risk (usually home dwelling) elderly people”.

Diseases and Drugs Associated With an Increased Risk of Generalized Osteoporosis in Adults#

Diseases	Nutritional Conditions	Drugs	Disorders Of Collagen Metabolism	Other
Hypogonadism Hyperadrenocorticism Thyrotoxicosis Anorexia Nervosa Hyperprolactinemia Porphyria Hypophatasia In Adults Diabetes Mellitus Type 1 Pregnancy Hyperparathyroidism Acromegaly	Inf Bowel Disease, Malabsorption Syndromes and Malnutrition Chronic Liver Disease Gastric By pass Operations Vit. D Deficiency Alcoholism Primary Biliary Cirrhosis	Vitamin D Toxicity Phenytoin Glucocorticoids* Depo-medroxyprogesterone Phenobarbitol Excessive Thyroid Medication Heparin Gonadotropin-Releasing Hormone Agonists Lithium Cancer Chemotherapy Cyclosporine A and tacrolimus Aromatase inhibitors	Osteogenesis Imperfecta Homocysinuria Due To Cystathionine Deficiency Ehler-Danlos Syndrome Marfan Syndrome	Rheumatoid Arthritis Myeloma And Some Cancers Immobilization End stage renal disease Renal Tubular Acidosis Hypercalciuria COPD Organ Transplantation Sickle Cell Anemia Mastocytosis Thalassemia Muscular dystrophy and disuse states

Not an exhaustive list
*Glucocorticoids (≥ 5 mg/d of prednisone or equivalent for ≥ 3 mo)

Diagnosing Osteoporosis –

A clinical diagnosis can often be made in at-risk individuals who sustain a low-trauma fracture. Alternatively, the diagnosis of osteoporosis is established by measurement of BMD.

BMD TESTING

Bone mineral density (BMD) measurement can be used to establish or confirm a diagnosis of osteoporosis, predict future fracture risk, and monitor changes in BMD due to medical conditions or therapy. BMD has a continuous, graded, inverse relationship to the risk of fracture: **The lower the BMD, the greater the risk**. Some patients (ie, those over 70 with multiple risk factors) are at sufficiently high risk for osteoporosis that treatment is warranted without BMD testing. The decision to test for BMD should be based on an individual's risk profile, and testing is never indicated unless the results could influence a treatment decision.

BMD TESTING TECHNIQUES

1. Dual-energy x-ray absorptiometry (DXA or DEXA). DXA can be used to measure bone mineral density in the spine, hip, or wrist—the most common sites for osteoporotic fractures. DXA scans can be completed in a few minutes with radiation exposure that is approximately one tenth that of a standard chest x-ray. This is the most reliable measurement for both men and women.

2. Single-energy x-ray absorptiometry (SXA) and peripheral dual-energy x-ray absorptiometry (pDXA or pDEXA). These techniques measure bone density in the forearm, finger, and sometimes the heel. Measurement by validated pDXA devices can be used to assess vertebral and overall fracture risk in postmenopausal women. There is lack of sufficient evidence for fracture prediction in men. pDXA is associated with exposure to trivial amounts of radiation. pDXA is not appropriate for monitoring BMD after treatment.

3. Radiographic absorptiometry (RA). RA is a technique that is based on a standard x-ray or computer-generated x-ray of the hand with a metal wedge in the same field. RA is similar in accuracy and precision to SXA.

4. Quantitative computed tomography (QCT). QCT measures trabecular and cortical bone density at several sites in the body, but is most commonly used to measure trabecular bone density in the spine and hip. It may be used as an alternative to DXA for vertebral measurements and to predict spinal fractures in post menopausal women. Peripheral QCT, (pQCT) which measures BMD at forearm or tibia, can predict hip but not spine fractures. There is lack of sufficient evidence for fracture predication in men with this technology. Radiation exposure is higher than with DXA or pDXA.

5. Quantitative Ultrasound densitometry (QUS). **Quantitative ultrasound densitometry (QUS)** does not measure BMD directly but rather speed of sound (SOS) and/or broadband ultrasound attenuation (BUA) at the heel, tibia, patella and other peripheral skeletal sites. A composite parameter using SOS and BUA may be used clinically. Validated heel QUS devices predict fractures in postmenopausal women (vertebral, hip and overall fracture risk) and in men 65 and older (hip and non-vertebral fractures). QUS is not associated with any radiation exposure.

Bone Mineral Density Measurement and Classification

Dual-energy x-ray absorptiometry (DXA) measurement of the hip and spine is the technology now used to establish or confirm a diagnosis of osteoporosis, predict future fracture risk and monitor patients by performing serial assessments.13 Areal BMD is expressed in absolute terms of grams of mineral per square centimeter scanned (g/cm2) and as a relationship to two norms: compared to the expected BMD for the patient's age and sex (Z-score), or compared to "young normal" adults of the same sex (T-score). The difference between the patient's score and the norm is expressed in standard deviations (SD) above or below the mean. Usually, 1 SD equals 10 to 15 percent of the BMD value in g/cm2. Depending upon the skeletal site, a decline in BMD expressed in absolute terms (g/cm2) or in standard deviations (T-scores or Z-scores) begins during young adulthood, accelerates in women at menopause and continues to progress in postmenopausal women and men age 50 and older (see Figure 3). The BMD diagnosis of normal, low bone mass, osteoporosis and severe or established osteoporosis is based on the WHO diagnostic classification
Although available technologies measuring central (spine and hip) and peripheral skeletal sites (forearm, heel, fingers) provide site-specific and global (overall risk at any skeletal site) assessment of future fracture risk, DXA measurement at the hip is the best predictor of future hip fracture risk.

In postmenopausal women and men age 50 years and older, the WHO diagnostic T-score criteria (normal, low bone mass and osteoporosis) are applied to BMD measurement by central DXA at the lumbar spine and femoral neck. BMD measured by DXA at the one-third (33 percent) radius site can be used for diagnosing osteoporosis when the hip and spine cannot be measured.

World Health Organization definitions based on BMD measurement at the spine, hip or forearm by DXA devices:

Bone Mass	Definition	T-Score
Normal	1 SD of a "young normal" adult	T-score above -1
Low bone mass (osteopenia)	between 1 and 2.5 SD below that of a "young normal" adult	T-score between -1 and -2.5
Osteoporosis	2.5 SD or more below that of a "young normal" adult. Patients in this group who have already experienced one or more fractures are deemed to have severe or "established" osteoporosis.	T-score at or below -2.5

- Although these definitions are necessary to establish the presence of osteoporosis, they should not be used as the sole determinant of treatment decisions.

Selecting Patients for BMD Testing

The decision to perform bone density assessment should be based on an individual's fracture risk profile and skeletal health assessment and the results should influence the treatment plan. BMD measurement is not recommended in children or adolescents and is not routinely indicated in healthy young men or premenopausal women.

Indications for BMD Testing:

- Women age 65 and older and men age 70 and older, regardless of clinical risk factors
- Younger postmenopausal women and men age 50 to 69 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 in a daily dose ≥ 5 mg prednisone or equivalent for ≥ three months) associated with low bone mass or bone loss
- Anyone being considered for pharmacologic therapy for osteoporosis
- Anyone being treated for osteoporosis, to monitor treatment effect

- Anyone not receiving therapy in whom evidence of bone loss would lead to treatment

Medicare covers BMD testing for many individuals age 65 and older, including but not limited to:

- Estrogen deficient women at clinical risk for osteoporosis
- Individuals with vertebral abnormalities
- Individuals receiving, or planning to receive, long-term glucocorticoid therapy in a daily dose ≥ 5 mg prednisone or equivalent for ≥ three months
- Individuals with primary hyperparathyroidism
- Individuals being monitored to assess the response or efficacy of an approved osteoporosis drug therapy

ADDITIONAL RISK ASSESSMENT WHO FRACTURE RISK ALGORITH (FRAX)

FRAX™ was developed to calculate the 10-year probability of a hip fracture and the 10-year probability of a major osteoporotic fracture (defined as clinical vertebral, hip, forearm or humerus fracture) taking into account femoral neck BMD and the clinical risk factors: age, gender, history of Rheumatoid arthritis, h/o prior fracture, parental history of hip fracture, current smoking, BMI, alcohol intake and prior use of glucocorticosteroids.

The FRAX™ algorithm is available at www.nof.org. The reader is referred to NOF Guideline and the site for additional details. Incorporation of the FRAX questionnaire should soon be available on newer DXA scanners.

Treatment:

Postmenopausal women and men age 50 and older presenting with the following should be considered for treatment:

- A hip or vertebral (clinical or morphometric) fracture
- T-score ≤ -2.5 at the femoral neck or spine after appropriate evaluation to exclude secondary causes
- Low bone mass (T-score between -1.0 and -2.5 at the femoral neck or spine) and a 10-year probability of a hip fracture ≥ 3% or a 10-year probability of a major osteoporosis-related fracture ≥ 20% based on the US-adapted WHO algorithm (FRAX)

All patients should be counseled on adequate calcium and Vitamin D intake. Lifestyle modifications should be made and secondary and contributing medical problems addressed.

Pharmacology: **FDA-approved pharmacologic options for osteoporosis prevention and/or treatment** in alphabetical order: bisphosphonates (alendronate, alendronate plus D, ibandronate, risedronate, risedronate with 500 mg of calcium carbonate and zoledronic acid), calcitonin, estrogens (estrogen and/or hormone therapy), estrogen agonist/antagonist (raloxifene) and parathyroid hormone [PTH(1-34), teriparatide].

The anti-fracture benefits of FDA-approved drugs have mostly been studied in women with postmenopausal osteoporosis. There are limited fracture data in glucocorticoid-induced osteoporosis and no fracture data in men.

See Table below.

Follow Up:

- Central DXA – measurements vary with machine and operator
- QCT

In general, follow up every two years per the Medicare guidelines, Some clinical situations may warrant a different interval.

Drug	Indication	Dosing	Outcomes	Special Considerations	Cost
Bisphosphonates					
Alendronate (Fosamax®)	Prevention Treatment	5 mg/day or 35 mg/wk 10 mg/day or 70 mg/wk	Reduces the incidence of fracture at the spine, hip, and wrist by about 50% over 3 yrs in patients with osteoporosis with or without prior spine fracture.	Must be taken on an empty stomach, first thing in the morning, with a large glass of water, at least 30 minutes before eating or drinking. Causes esophageal irritation. Patients should remain upright during this interval. Cannot be taken at the same time as calcium as it hinders absorption. Approved for treatment of increased bone mass in men and women with both osteoporosis and osteoporosis from glucocorticoids	$$$$$
Alendronate + D (Fosamax® + D)	Treatment	70 mg/wk with 2800 IU vitamin D_3			$$$$$
Ibandronate oral (Boniva®)	Prevention and Treatment	2.5 mg daily tablet 150 mg/month	Reduces the incidence of spine fractures by about 50% over 3 yrs.	Should be taken on the same day each month, at least 60 minutes before the first food, drink (other than water) or medication of the day. Must be taken on an empty stomach, first thing in the morning with a glass of water. Patients must remain upright for at least 60 minutes after taking medication.	$$$$$
Ibandronate IV (Boniva®)	Treatment	3 mg every 3 months administered over a period of 15-30 seconds	No data	Intended for intravenous administration only. Should not be administered in patients with severe renal impairment (SCr >2.3 mg/dL) or CrCl < 30 mL/min. Jaw osteonecrosis has been reported with intravenous bisphosphonates. Most common side effects are flu-like symptoms.	
Risedronate (Actonel®)	Prevention and Treatment	5 mg/day or 35 mg/wk 5 mg/day or 35 mg/wk 75 mg tablet on two consecutive days 150 mg tablet once a month	Risedronate reduces the incidence of spine fractures by 41-49% and non-spine fractures by 36% over 3 yrs in patients with a prior spine fracture.	Avoid with renal insufficiency. Cannot be taken at the same time as calcium as it hinders absorption. Must be taken on an empty stomach, first thing in the morning, with a large glass of water, at least 30 minutes before eating or drinking. Approved for treatment of increased bone mass in men and women with both osteoporosis and osteoporosis from glucocorticoids Actonel with Calcium is a co-package product containing Actonel (risedronate sodium tablets, 35 mg) which are taken	$$$$$

Drug	Indication	Dosing	Outcomes	Special Considerations	Cost
				once weekly and calcium carbonate tablets which are taken the remaining 6 days of the week. The calcium tablets may interfere with the absorption of risedronate and should not be taken at the same time as risedronate tablets.	
Risedronate with Calcium (Actonel® with Calcium)		35 mg/wk with 6 tablets of 500 mg calcium carbonate each			
Zoledronic acid (Reclast®)	Treatment	5 mg by IV infusion over at least 15 min once a year	Reduces the incidence of vertebral fractures by about 70%, hip fractures by about 41% and non-vertebral fractures by 25% over 3 years.	Patients may be pretreated with acetaminophen to reduce the risk of an acute phase reaction (arthralgia, headache, myalgia, fever) which occur 32% after first dose and 7% after 2nd dose and 3% after 3rd dose.	
Calcitonin					
Calcitonin (Miacalcin®)	Treatment	Single daily intranasal spray providing 200 IU of the drug Also available in SQ and oral dosage form	May reduce risk of vertebral fracture by 33%.	Indicated for women who are at least 5 years postmenopausal. Calcitonin is generally considered to be a safe but somewhat less effective intervention for osteoporosis. Causes esophageal irritation. Can cause rhinitis and epistaxis.	$$$$$
Estrogen/Hormone Therapy					
HRT	Prevention		Women's Health Initiative found 5 yrs of one of the HRT (Pempro) reduced risk of vertebral and hip fractures by 24% and other fracture by 23%.	Since HRT may be associated with a modest increase in risk of breast cancer with long-term use and deep vein thrombosis, women with a history of, or at significant risk for, these conditions may be exceptions.	$$
Parathyroid Hormone					
Teriparatide (Forteo®)	Treatment	20 ug daily SQ	Reduces risk of spine fractures by 65% and other fractures by 53% after 18 mo of therapy .	To be used in postmenopausal women with high risk of fracture. Also to increase bone mass in men with primary or hypogonadal osteoporosis at high risk of fracture Available as a 3 mL pen which holds 28 doses. One pen can be used for 28 days and then must be discarded. Osteosarcoma in animal models has been reported and therefore should not be administered to people having a	$$$$$

Drug	Indication	Dosing	Outcomes	Special Considerations	Cost
				baseline risk for developing this condition. (Pagets, prior RT, et al.) Max use 2 years. Safety and efficacy not been demonstrated beyond 2 yrs of treatment.	
Selective Estrogen Receptor Modulator					
Raloxifene (Evista®)	Prevention and Treatment	60 mg/day	Reduces the risk of spine fracture by 30% in patients with and by 55% in patients without a prior spine fracture, over 3 yrs.	Raloxifene increases the risk of deep vein thrombosis to a degree similar to that observed with estrogen. In addition, an increase in hot flashes is observed (~6% over placebo). May cause an increase chance of uterine cancer.	$$$$$

HRT or estrogen replacement therapy should be considered for menopausal symptoms but should not be used to treat only osteoporosis unless all other modalities have been exhausted.

Patient Education:

Clinical Reference System- Adult and Women's Health Advisor both have information related to Osteoporosis that can be used for patient information. Other sources of patient information can be obtained through WEB at www.nof.org.
Counsel all patients on the risk factors for osteoporosis. Osteoporosis is a "silent" risk factor for fracture; one out of two white women will experience an osteoporotic fracture at some point in her lifetime. All women should be counseled on the following 3 basic preventive guidelines:

1. ADEQUATE INTAKE OF CALCIUM AND VITAMIN D: Advise all patients to obtain an adequate intake of dietary calcium (at least 1200 mg/d, including supplements if necessary) and vitamin D_3 (400 to 800 IU per day for individuals under age 50, and 800-1,000IU for adults age 50 and older). Vitamin d3 is the form of vitamin D that best supports bone health. Vitamin D can be obtained from fortified milk, egg yolks, saltwater fish, liver and supplements.

2. REGULAR WEIGHT-BEARING EXERCISE: Recommend regular weight-bearing and muscle-strengthening exercise to reduce the risk of falls and fractures. Includes walking, jogging, stair climbing, dancing, and tennis. Weight lifting improves muscle mass and bone strength.

3. AVOIDANCE OF TOBACCO USE AND ALCOHOL ABUSE: Advise patients to avoid tobacco smoking and to keep alcohol intake moderate.

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