

OSTEOPOROSIS

A Resource from the American College of Preventive Medicine

A Clinical Reference

The following Clinical Reference provides evidence to support the Osteoporosis Time Tool.

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1. DESCRIPTION / DEFINITION

Osteoporosis, or porous bone, is a disease characterized by low bone mass and structural deterioration of bone tissue, leading to bone fragility and an increased susceptibility to fractures, especially of the hip, spine and wrist, although any bone can be affected. [1]

- In simpler terms, osteoporosis is a condition in which the bones become weak and can break from a minor fall or, in serious cases, from a simple action such as a sneeze.
- It is a silent disease. People cannot feel their bones getting weaker. They may not know that they have osteoporosis until they break a bone.

The commonly used definition of osteoporosis, from the World Health Organization (WHO), is a BMD more than 2.5 standard deviations (SD) below the mean for a young healthy adult woman. [2]

- Osteopenia is a BMD between 1 and 2.5 SD below the mean.

It is a major public health concern that places an enormous medical and personal burden on individuals and their families, and on the health care system.

- Guidelines emphasize the importance of using bone mineral density (BMD) testing and risk factor assessment to identify patients at high risk for fracture before the first fracture occurs. [3,4]

A person with osteoporosis can fracture a bone from a minor fall, or in serious cases, from a simple action such as a sneeze or even spontaneously. [3]

- Fractures due to osteoporosis are most likely in the hip, spine and wrist, but any bone can be affected.
- Vertebral (spinal) fractures may initially be felt or seen in the form of severe back pain, loss of height, or spinal deformities such as kyphosis or stooped posture. In many cases, vertebral fractures occur with no pain.

2. PREVALENCE

Osteoporosis is a major health threat for an estimated 44 million Americans, or 55% of people 50 years of age and older. [1]

- 10 million individuals are estimated to already have the disease and at least 34 million more to have low bone mass, placing them at increased risk for osteoporosis. [1]

It is primarily a women's disease, especially postmenopausal women. [1]

- Of the 10 million Americans estimated to have osteoporosis, 80% (eight million) are women.
- Women can lose up to 20% of their bone mass in the 5-7 years after menopause, making them more susceptible to osteoporosis. [1]
- About 1 in every 6 postmenopausal women has osteoporosis of the lumbar spine. [5]

Note: Men's rates of osteoporosis do increase to near those of women as they get older and complications and mortality related to hip fractures is 3 times higher in men than women.

The prevalence of osteoporosis or low bone mass in women over 50, by ethnicity: [1]

Ethnicity	With Osteoporosis	With Low Bone Mass
Non-Hispanic white	20%	52%
Asian	20%	52%
Hispanic	10%	49%
Non-Hispanic black	5%	35%

Another analysis suggested that the prevalence may be even higher in women over 50. [6]

Ethnicity	Osteoporosis	Low Bone Mass	Total Affected
Non-Hispanic white and Asian	20%	50-65%	70-85%
Hispanic	10-15%	49-56%	59-71%
Non-Hispanic black	5-10%	35-38%	40-48%
Native American	12%	45%	57%

Prevalence increases with age.

- Large population-based surveys have shown that approximately 30% of people over age 65 years have osteoporosis. [7]

The number actually diagnosed and treated for osteoporosis is only a fraction of the total number afflicted. [3]

- Osteoporosis is called a silent disease because it occurs without visible signs or symptoms, often until a fracture occurs. It cannot be diagnosed by laboratory tests or physical examination, usually only by a DXA scan or a fracture (often low impact).

Many more are at risk for osteoporosis.

- In a community sample of healthy women 50 to 65 years of age who had DXA scans, over half were abnormal. [8]

An osteoporosis screening service in a community pharmacy that screened 444 women over 48 months found that:

- 83% had at least one modifiable risk factor, and according to the bone density tests, 58% were at high risk for osteoporosis and 26% were at moderate risk. [9]
- Only 14% were classified as low risk.

Many women underestimate osteoporosis.

The majority of women believe that osteoporosis is a serious condition, but are less concerned about it than cancer, cardiovascular disease, and neurologic disorders. [10]

- Only 29% perceived a personal susceptibility to osteoporosis, and only 40% were taking active measures to prevent osteoporosis.

Many fragility fracture patients do not associate their fracture with osteoporosis. [11]

- An analysis of 127 fragility fracture patients found that an osteoporosis diagnosis was reported in only 44%, and only 17% thought their fracture was related to osteoporosis.
- Less than half perceived themselves at increased risk of another fracture.
- The only factor significantly associated with the perception that the fracture was related to osteoporosis was a diagnosis of osteoporosis.
- It is crucial for physicians to communicate to patients the presence of osteoporosis and the impact on the present and future fractures.

Misconceptions about osteoporosis risk and protective factors persist. [12]

- Nearly 2 out of 3 women (aged 40-86) in a community sample rated their perceived risk of osteoporosis as lower than other women their age; fewer than 1 in 6 perceived it as higher. Only half and a third of the women mentioned calcium consumption and exercise, respectively, as protective factors employed to reduce osteoporosis risk.

3. FRACTURE INCIDENCE AND IMPACT

About half of Caucasian, Asian and Hispanic women and a third of African American women over 50 will experience an osteoporosis-related fracture in their lifetime. [3]

- About 1 in 4 will develop a vertebral deformity [13] and greater than 1 in 7 will suffer a hip fracture. [14]
- Risk increases steadily as bone density declines, with no threshold.
- A woman's risk of hip fracture is equal to her combined risk of breast, uterine and ovarian cancer.
- Women with a hip fracture are at a four-fold greater risk of a second one. [1]

According to figures from the NOF, osteoporosis was responsible for more than 2 million fractures in 2005, including approximately: [1]

- 297,000 hip fractures
- 547,000 vertebral fractures
- 397,000 wrist fractures
- 135,000 pelvic fractures
- 675,000 fractures at other sites

Impact on morbidity and mortality:

Nearly 1 in 4 hip fracture patients aged 50 and over will die within a year of their fracture; vertebral fractures are also linked to an increased risk of death as a result of complications of the fracture, surgery or hospitalization. [1]

- One in five who were ambulatory before their hip fracture require long-term care afterward. [1]
- Only 2 in 5 will regain their pre-fracture level of independence. [3]
- At six months after a hip fracture, only 15% can walk across a room unaided. [1]

Potential Effects of Osteoporosis Related Fractures [15-20]

General

- Pain -- acute or chronic
- Depression
- Reduced self-esteem
- Social isolation
- Fear, anger, anxiety

Hip Fracture

- Increased mortality, 10% to 20% increased deaths in the year following hip fracture
- Increased risk for other osteoporosis-related fractures -- approximately 10% have a second fracture within a year of the incident hip fracture
- 60% of those who survive hip fracture do not regain the same level of independence
- 25% of those who survive hip fracture require long-term nursing home care

Vertebral Fracture

- Height loss
- Kyphosis
- Respiratory and gastrointestinal problems due to skeletal position changes
- Limited ability to stretch to reach objects or bend over

Economic Impact of Fractures

- Over \$17 billion annually in direct medical costs
- Over 430,000 hospital admissions annually
- Approximately 2.5 million medical visits each year
- Over 180,000 annual admissions to nursing homes
- Lost income due to incapacitation, morbidity, and mortality risks

4. ETIOLOGY

The bony skeleton is a remarkable organ that serves both a structural function and a reservoir function, as a storehouse of essential minerals, notably calcium. [3]

- Much of the cellular activity in bones consists of removal and replacement at the same site, a process called remodeling. The remodeling process occurs throughout life so that most of the adult skeleton is replaced about every 10 years.
- The growth of the skeleton, its response to mechanical forces, and its role as a storehouse of minerals all depend on the proper functioning of hormones that respond to changes in blood calcium and phosphorus; if either are in short supply, the regulating hormones take them out of bone to serve other functions.

Osteoporosis occurs when the normal processes of bone turnover are out of balance and osteoclast activity (cells responsible for breakdown of old bone tissue) exceeds osteoblast activity (cells responsible for building new bone tissue). [16]

- Over time, trabecular thinning and reductions in trabecular horizontal connections cause loss of bone strength and predisposes the bone to fracture.
- Osteopenia is the same as osteoporosis except that there is less severe compromise in bone strength.

Lifelong adequate calcium and vitamin D intake is necessary for the acquisition of peak bone mass and subsequent maintenance of bone health. [15]

- The skeleton contains 99% of the body's calcium stores; when the exogenous supply is inadequate, bone tissue is resorbed from the skeleton to maintain serum calcium at a constant level.

5. PRACTICE PATTERNS

There is evidence that a large majority of women of menopausal or postmenopausal age understand the importance of osteoporosis and want to discuss it with their physicians, but that such discussions are not happening often enough.

- In one survey, 92% rated such a discussion as important, but only 44% had had such a discussion. [21]
- Another study found that 75% of American women between the ages of 45 and 75 years have never discussed osteoporosis with their physician. [22]
- Less than half (46%) of women between 18 and 65 years reported discussing osteoporosis with their providers during their annual health maintenance examination, and half (51%) reported discussing calcium intake (which is recommended by the USPSTF for all women over 18). [23]
- There is great variability in rates of addressing these issues. One analysis found that some physicians include a discussion of osteoporosis in 90% of annual well woman exams, but overall only about half did so. [23]
- A review of 263 charts of women over 50 from 3 residency clinics found that only a third contained documentation of some discussion of osteoporosis. [24]
- Female physicians discussed osteoporosis more than their male colleagues. [24]
- Discussions of osteoporosis actually declined with increasing patient age as absolute risk increased. [24]

Rates of counseling about osteoporosis are lower in minority women.

- Only 13% of low-income postmenopausal Mexican-American women recalled such a discussion with their health care provider. [25]

Under-diagnosis remains a problem.

Studies show that physicians frequently fail to diagnose osteoporosis, even in elderly who have suffered a fracture. [3,26,27]

- A review of osteoporosis diagnosis data for white women aged 60 years and older from the National Ambulatory Medical Care Surveys (1993-1997) found that fewer than 2% of the women received diagnoses of osteoporosis, although the expected prevalence was 20% to 30%. [28]
- Only one third of vertebral fractures, the most common type of osteoporotic fracture, are clinically recognized, and many fractures that are present on radiographs are not identified in radiology reports or summaries. [3]

Bone density testing is under-used.

National osteoporosis clinical guidelines for screening recommend BMD testing in average risk women beginning at age 65. [2,15]

- A random sample of women, aged > 65, in a large multisite primary-care group practice serving over 180,000 patients with 13 practice locations, 34 physicians, in either family medicine or internal medicine showed that:
 - Physician-specific osteoporosis screening rates varied widely, ranging from 19% to 97%.
 - Practice-specific osteoporosis screening rates ranged from 26% to 91%.
 - Overall, the mean rate of osteoporosis screening among all physicians was 56% in this group that is recommended to be screened by all major medical organizations. [29]
- Another analysis of primary care physicians found that the percentage who order bone density tests to screen for osteoporosis in postmenopausal women varied from 38% to 62%. [30]
- A cross-sectional survey of nearly 500 primary care physicians found that 25% of them reported fewer than 4 referrals for BMD testing per month. [31]
- Only half over age 65 had received a BMD test (which is unanimously recommended). [21]
- After Medicare began reimbursing BMD testing in 1999, fewer than 1 in 4 eligible women had received testing in the subsequent two years. The likelihood of being tested declined with age, even after adjusting for race, risk factors, SES and co-morbidities. [32]

Higher risk patients do not seem to be tested more frequently.

Higher risk patients are not being identified and recommended for more aggressive assessment and intervention. Surveys of patients and medical records show that less than half of patients who are at high risk for fractures are being recommended to have DXA scans. [33, 34]

- An analysis of four Midwestern health systems showed that only 1 to 2 of every 8 patients who suffer hip fractures had their bone density tested. [35]
- Other studies have confirmed the low rates (3% to 23%) of bone density testing in high risk patients. [36,37]

Secondary causes are not routinely assessed.

More women are now being screened with DXA than ever before. But providers ordering DXAs are often not pursuing a workup for secondary causes. [38]

- Vitamin D deficiency/insufficiency and primary hyperparathyroidism is often present and should be treated first.
- Secondary causes need to be recognized before the typical reflexive response of prescribing an antiresorptive agent.

Even with a diagnosis of osteoporosis, treatment is often inadequate.

- Only 58% of diagnosed patients were taking prescription osteoporosis-related medications, and 61% were taking prescription medications or calcium or both. [33]
- Less than one quarter of women 60 and older who were diagnosed with a fracture of the hip, vertebra, or wrist received drug treatment for osteoporosis within the year following the fracture.[39]
 - Increasing age was associated with a lower likelihood of being treated.
- An analysis of four Midwestern health systems showed that fewer than 1 in 4 hip fracture patients were given calcium and vitamin D supplements and less than 1 in 10 were treated with antiresorptive drugs. [35]
- Other studies have confirmed the low rates of calcium/vitamin D supplementation (11% to 44%) and antiresorptive therapy (12% to 16%) in high risk patients. [36,37]
- Rates of osteoporosis treatment 1 year after sustaining a fracture are less than 10% to 20%. [40]

Osteoporosis is especially under-diagnosed and under-treated in women of racial/ethnic minority groups. [6, 42, 43]

- In a comparison of white and black women with low BMD detected on initial bone scan, only 61.9% of black women compared with 83.3% of white women were treated. [42]

Studies have consistently shown that black women are not screened for osteoporosis or treated as aggressively when they are diagnosed as white women. It may be because of a perception that the disease is less serious in black women. [44, 45]

- It is true that African-American women have a lower prevalence of osteoporosis, but they experience greater disability, longer hospital stays, and higher mortality rates from it than white women.
- A survey of women 50 years of age and older enrolled in a large regional HMO (n = 8,909) showed that black women had two- to threefold lower odds of BMD test or osteoporosis prescription treatment. Even among women with a previous fracture, blacks still had a significantly lower likelihood of both BMD testing and prescription therapy. [45]
- In another study, a random sample of 400 women aged 45 years and older in a family medicine community-based research network showed that, compared with black women, white women were 6 times as likely to have had a past bone density test, 3 times as likely to have discussed osteoporosis with their doctor, and 2.4 times as likely to have a physician recommendation to take calcium. [46]
- A chart review at an urban academic hospital and a suburban community hospital showed that significantly fewer African-American than white women were referred for a DXA scan (OR 0.39). [44]
- Physicians were also less likely to mention consideration of osteoporosis in medical records (0.27) and to recommend calcium and vitamin D supplementation for this population (0.21). [44]

Lack of follow-up.

There is a significant problem with compliance with pharmacologic therapy when it is prescribed.

- Despite the reduction in fracture risk of 40-60%, many take their medication incorrectly or do not take it long enough to achieve the full benefit. [47]

There is some promise of improvements in practice.

There has been a five-fold increase in office visits for osteoporosis (from 1.3 to 6.3 million) in the past 10 years. [1]

The National Osteoporosis Risk Assessment (NORA) study began in 1998, evaluating the osteoporosis management practices of 2800 physicians. 808 were available for follow-up 8 years later. [48]

From 1998 to 2006:

- The percentage using BMD testing "often" more than doubled - from 35% to 87%.
- the percentage who reported that a T-score of -2.5 was the threshold for osteoporosis doubled - from 34% to 67%.
- The percentage who used bone turnover markers to screen, diagnosis, or monitor osteoporosis almost tripled (19% to 55%).
- The percentage of patients prescribed or recommended hormone therapy dropped six-fold (67% to 11%).
- The percentage of patients prescribed bisphosphonates increased fourfold (15% to 59%).

6. DIAGNOSIS

The diagnosis of osteoporosis is established by a BMD measurement. A clinical diagnosis can also be made in at-risk individuals who sustain a low trauma fracture. [15]

Clinical Diagnosis

Can be made in the presence of a fragility fracture, often defined as a fracture occurring with no obvious trauma or minimal trauma, such as a fall from the standing position. [15]

- BMD testing is necessary to identify reduced bone density as the cause and to confirm a diagnosis of osteoporosis or osteopenia.

BMD Measurement

Dual-energy x-ray absorptiometry (DXA) of the hip and spine is the technology recommended by the World Health Organization used to establish or confirm a diagnosis, predict fracture risk and monitor patients over time. [15, 49]

- It is clinically proven, noninvasive, takes only 10-15 minutes, and exposes patients to less than a tenth the radiation of a chest x-ray.
- The disadvantages are that the machine is not portable (mobile units are available in some areas), and it does not provide any information about bone architecture.
- It must be done by properly trained personnel, using a properly maintained instrument in order to get a valid measurement.
- In postmenopausal women, the diagnosis is made based on measurements at the lumbar spine and femoral neck.
- The International Society for Clinical Densitometry (ISCD) recommends that diagnosis be based on the lowest T-score from the posterior-anterior lumbar spine (L1-L4), total proximal femur, femoral neck, or, in certain circumstances the 33% radius (if measured). [50]

It is expressed in absolute terms - grams per square cm, and is then related to one of two norms:

- The expected BMD for the patient's age and gender (Z-score) for younger pre-menopausal, or
- The expected BMD of a "young normal" adult of the same gender (T-score) for women in the transition or postmenopausal.

The difference is expressed in standard deviation (SD) units above or below the mean.

- Usually one SD equals about 10-15% of the BMD value
- Each decrease of a standard deviation represents a doubling of fracture risk. [51]
- The number of SD units above or below the mean is used to classify the BMD as normal, low bone mass, osteoporosis, or severe osteoporosis.

BMD classifications using T scores are: [52]

T-score	Interpretation
-1.0 or higher (i.e., within one SD of a "young normal" adult)	Normal
-1.1 to -2.4 (at least 1 SD but less than 2.5 SD below that of a "young normal" adult)	Osteopenia
-2.5 or lower (at least 2.5 SD below that of a "young normal" adult)	Osteoporosis
-2.5 or lower, with low trauma fracture(s)	Severe osteoporosis

It is the only BMD measurement technology that can be used with the recently developed WHO fracture risk assessment tool, FRAX. [53]

The WHO FRAX™ algorithm can be used to calculate the 10-year probability of major osteoporotic fracture (spine, hip, humerus, or forearm) or hip fracture. It is available at www.nof.org and at www.shef.ac.uk/FRAX

- In addition to BMD (entered as DXA-measured T-score of the femoral neck), FRAX uses age, height, weight, sex, previous fracture, parent with hip fracture, current smoking, glucocorticoid use, rheumatoid arthritis, secondary osteoporosis, and alcohol intake of 3 or more units per day as clinical risk factors.
- It is most useful in patients with low hip BMD. It has not been validated for the use of spine BMD.
- Clinicians need to use clinical judgment in this situation, since FRAX™ may underestimate fracture risk in these individuals based on the exclusive use of femoral neck BMD.

FRAX has been validated in postmenopausal women and men age 50 and older who have not received pharmacologic therapy for osteoporosis. [15]

- It should not be used in other patients.
- Can be used to identify patients for whom treatment to reduce fracture risk is likely to be cost-effective.^[3]

Calcaneal Ultrasound – Some Advantages but Lacking Accuracy

An alternative screening test is calcaneal quantitative ultrasound (QUS). [54]

- It has the advantage of being portable, involves no radiation, and is relatively inexpensive.
- However, it has been shown to have poor sensitivity for detecting osteoporosis (21% to 45%).

Biochemical markers

Biochemical markers of bone formation and resorption are also available, however there are no established guidelines for their use in diagnosis or treatment monitoring. [55]

- Markers of formation include bone-specific alkaline phosphatase, osteocalcin, and procollagen I carboxy and N-terminal extension peptides.
- Markers of resorption include urinary levels of pyridinolines and deoxypyridinolines, and serum and urine levels of type 1 collagen telopeptides.
- These markers may be helpful in monitoring response to therapy, but are not useful in predicting bone mass or estimating fracture risk.

Importance of BMD Testing

An increase in BMD testing and osteoporosis treatment has been associated with a decrease in hip fracture incidence. [1]

- Medicare reimburses BMD testing every two years.

There is no "fracture threshold" for BMD below which a fracture is certain to occur but rather a continuum of increasing fracture risk as BMD decreases.

- Biomechanical studies show a strong association between mechanical strength and BMD measured by DXA. [56]
- Epidemiologic studies show a strong relationship between increasing fracture risk and declining BMD measured by DXA. [57]
- There is a relationship between reduction in fracture risk with pharmacologic therapy and increases in BMD measured by DXA. [59]

Indications for BMD Testing:

The 2008 National Osteoporosis Foundation (NOF) Clinical Guidelines recommend that all postmenopausal women older than age 65 should be evaluated by DXA because of the very high risk for osteoporosis in this group. [15]

- Postmenopausal women younger than age 65 who have clinical risk factors should also be evaluated.

NOF 2008 Recommendations for BMD Testing [15]

- All women \geq 65 years, regardless of their risk profile
- Postmenopausal women $<$ 65 with a concerning clinical profile
- Perimenopausal women with a particular risk factor for fracture
- Anyone under consideration for osteoporosis medication therapy
- Any adult taking high-risk medication or who has a high-risk condition for bone loss
- Any adult $>$ 50 years who sustains a fracture
- Postmenopausal women who are coming off estrogen therapy
- Anyone in whom knowledge of low BMD would lead to pharmacotherapy
- To monitor effectiveness in anyone taking pharmacologic therapy

The determining factor for ordering a BMD test, as with any diagnostic or screening test, is the likelihood that the results would influence patient management decisions.

- It is not recommended as a screening test in healthy premenopausal women, perimenopausal women without risk factors, or postmenopausal women under age 65 without risk factors because the results are unlikely to influence management.

Medicare Coverage

Biennial BMD testing is covered by Medicare for individuals with a broad range of risk factors for osteoporosis, including any of the following:

- age 50 or older
- women
- a family or personal history of broken bones
- Caucasian or Asian ethnicity
- small-boned
- low body weight (less than about 127 pounds)
- smoke or drink a lot
- low-calcium diet

<http://www.medicare.gov/Health/osteoporosis.asp>

Relying solely on BMD testing will miss many women at risk for fracture.

- DXA results only indicate BMD; they do not evaluate bone quality, clinical risk factors, or fall risk.
- BMD can predict fracture risk, [51, 57, 62, 63] BUT a better predictor is BMD combined with clinical risk factors for fracture. [15,64]
- BMD alone may underestimate or overestimate fracture risk because it does not consider important risk factors that are independent of BMD, such as age and previous fragility or low-trauma fracture.
- Combining BMD with clinical risk factors provides a better estimate of fracture risk than BMD or risk factors alone. [65]

Some fractures occur at BMD levels below the threshold for osteoporosis.

- The National Osteoporosis Risk Assessment (NORA) study cohort of almost 150,000 postmenopausal white women showed that 82% of those with fractures had T-scores greater than -2.5 at peripheral skeletal sites. [66]
- The Study of Osteoporotic Fractures found that 54% of postmenopausal women with incident hip fractures did not have an osteoporotic T-score at the hip on DXA. [67]

Comprehensive risk assessment includes: [15]

- A complete history and physical examination, with laboratory testing for any suspected causes of secondary osteoporosis, e.g., multiple myeloma or osteomalacia.
- Evaluation of signs of subclinical fracture (e.g., height loss, back pain, kyphosis).
- Assessment of calcium and vitamin D deficiencies – testing serum calcium, 24-hour urinary calcium, and serum 25-OH-D (vitamin D).

- Note: Serum calcium may be normal in an individual who is calcium deficient. This is because low serum calcium triggers PTH release which increases bone resorption, increases calcium absorption by the digestive tract and increases calcium retention by the kidneys. These mechanistic actions result in normalization of serum calcium levels. The best determinant of calcium deficiency is 24-hour urine calcium. If low serum calcium is detected, the cause should be identified and treated before prescribing an anti-resorptive agent.
- Assessment of clinical risk factors (next section).

Evaluation of Secondary Causes

- Osteoporosis has been shown to be secondary to another condition in nearly a third of postmenopausal women. [68]
- Disorders of calcium metabolism and hyperparathyroidism were the most frequent diagnoses, followed by vitamin D deficiency. [68]

Secondary causes include: [69]

- Drugs
 - Steroids
 - Heparin
 - Medroxyprogesterone acetate (eg, Depo-Provera)
 - Anticonvulsants
 - Cytotoxic chemotherapy
 - Thiazolidinediones
 - Loop diuretics
 - Selective serotonin receptor inhibitors
 - Aromatase inhibitor therapy
- Hyperthyroidism
- Hypogonadism: premature menopause or amenorrhea lasting longer than 6 months
- Hyperparathyroidism
- Hypercortisolism
- Hypercalciuria
- Malabsorption: celiac disease, inflammatory bowel disease, after gastrectomy
- Liver disease (for example, primary biliary cirrhosis)
- Renal disease
- Malignancies and myeloproliferative disorders
- Connective tissue disorders
- Inherited disorders (osteogenesis imperfecta, Ehlers-Danlos syndrome, Marfan syndrome)
- Vitamin A in excess
- Neurological conditions (e.g. stroke, Parkinson's disease)

Tests to exclude secondary causes of osteoporosis: [69]

- Complete blood count
- Serum calcium (correct for albumin)
- Serum phosphate
- Total alkaline phosphatase
- Serum creatinine
- Serum protein electrophoresis
- Serum parathyroid hormone
- Serum thyrotropin hormone (TSH)
- Serum glucose (24 hour urine cortisol if indicated)
- Serum 25-hydroxy-vitamin D level
- Liver function tests
- 24 hour urine calcium level or spot calcium-creatinine ratio (if indicated)

7. CLINICAL RISK FACTORS

Some people are more likely to develop osteoporosis than others due to the presence of risk factors. They may be divided into modifiable and non-modifiable. Each modifiable risk factor needs to be assessed and modified as much as possible through patient education and counseling.

Risk Factors for Osteoporosis and Fracture: [3, 15]

Potentially Modifiable Factors	Difficult or Impossible to Modify Factors
<p>Lifestyle Factors</p> <ul style="list-style-type: none"> ▪ Excessive intake of vitamin A ▪ Alcoholism/high intake (≥ 3 drinks/day) ▪ Low intake of calcium ▪ Vitamin D deficiency ▪ Low activity/inactivity/immobility ▪ Smoking (passive or active) ▪ Small and thin - Weight ≤ 127, BMI ≤ 22 <p>Medication Use</p> <ul style="list-style-type: none"> ▪ Aluminum intake (eg, antacids) ▪ Aromatase inhibitor treatment ▪ Corticosteroid treatment <p>Physiologic Factors</p> <ul style="list-style-type: none"> ▪ Low sex hormones <ul style="list-style-type: none"> ○ Low estrogen levels in women, including menopause ○ Missing periods (amenorrhea) ▪ Eating disorder (anorexia nervosa) <p>Environmental Factors</p> <ul style="list-style-type: none"> ▪ Passive smoke exposure ▪ Risks for falls (eg, trip hazards, obstacles, ice) 	<p>Gender</p> <ul style="list-style-type: none"> ▪ Female <p>Race</p> <ul style="list-style-type: none"> ▪ Caucasian ▪ Asian <p>Physiologic Factors</p> <ul style="list-style-type: none"> ▪ Advanced age ▪ Rheumatoid arthritis ▪ Endocrine disorders (eg, Cushing's, thyroid abnormalities, diabetes, adrenal insufficiency, hyperparathyroidism) ▪ Gastrointestinal disorders (eg, malabsorption, inflammatory bowel disease, celiac disease, chronic liver disease) ▪ Hematologic disorders (hemophilia, sickle cell disease, thalassemia, leukemia, multiple myeloma) ▪ Renal disease (hypercalciuria, chronic kidney disease) ▪ Respiratory disease (COPD) ▪ Medical conditions predisposing to falls ▪ History of broken bones ▪ Complete inability to bear weight (e.g., paraplegia) <p>Family History</p> <ul style="list-style-type: none"> ▪ Family history of osteoporosis or hip fracture ▪ Genetic disorders (eg, cystic fibrosis, homocystinuria, Gaucher's disease, hemochromatosis, Marfan syndrome) <p>Medication Use</p> <ul style="list-style-type: none"> ▪ High risk medication use (eg, corticosteroids for ≥ 3 months, heparin, anticonvulsants, chemotherapeutic agents, depo-medroxyprogesterone)

The presence of risk factors may suggest the need for bone density testing. [15]

- Presence of modifiable risk factors should trigger recommendations for lifestyle modifications.
- All patients should be counseled on the importance of regular physical activity, including weight-bearing and resistive exercises to increase bone strength, and maintaining an adequate intake of calcium and vitamin D.

The most robust risk factors are advancing age, low body weight and personal history of fragility fracture.

- Risk for osteoporosis increases steadily and substantially with age. Relative to women aged 50-54, the odds of having osteoporosis were 5.9-fold higher in women aged 65-69 and 14.3-fold higher in women aged 75-79, in a study of over 200,000 postmenopausal women. [63]
- Low body weight (weight < 70 kg) has been shown to be the single best predictor of low bone mineral density. Low weight and no current use of estrogen therapy are incorporated with age into the 3-item Osteoporosis Risk Assessment Instrument (ORAI). [71,72]
- Other risk factors for fracture or low bone density found in some, but not all, studies include white or Asian ethnicity, history of fracture, family history of osteoporotic fracture, history of falls, low levels of physical activity, smoking, excessive alcohol or caffeine use, low calcium or vitamin D intake, and the use of various medications. [2]

A recent systematic review found that, in healthy women 40-60 years of age, there is good evidence to support only low body weight (< 70 kg) and post-menopausal status as risk factors for low BMD. [70]

- There was good or fair evidence that alcohol and caffeine intake, and reproductive history are **not** risk factors.
- And, there was inconsistent or insufficient evidence for the effect of calcium intake, physical activity, smoking, age at menarche, history of amenorrhea, family history of OP, race and current age on BMD.

8. COMMUNICATING RISK

Absolute risk (AR) is best for evaluating a patient's risk. [73]

- The probability of fracture over a specified period of time, e.g., a 10% 10-year risk of hip fracture.
- A 10-year time frame is more impactful than lifetime risk because people tend to think lifetime means toward the end of life, which they assume is a long time away.
- Relative risk is not so useful for estimating individual risk.

Relative risk (RR) is the ratio of AR of 2 populations, usually untreated patients with low BMD compared with an age-matched population with normal BMD (T-score = 0.0) or average BMD (Z-score = 0.0).

- If the low BMD group has a 10-year fracture risk of 10% and the age-matched average BMD group has a 10-year risk of 5%, then the $RR = .10/.05 = 2.0$.
- RR must always include a description of the comparison population.

Fracture risk in prospective cohort studies is commonly expressed as the RR of fracture for every 1 SD decrease in BMD.

- In a meta-analysis of 11 prospective cohort studies, the RR/SD decrease in BMD was 2.3 for lumbar spine BMD predicting vertebral fractures and 2.6 for proximal femur BMD predicting hip fractures. [57]

If a clinical trial of an intervention to prevent fractures shows a 10% 3-year risk of fracture in the control group and a 4% 3-year risk of fracture in the treated group, then the RR of fracture with treatment = $.04/.10 = 0.4$ (a 60% reduction in fracture risk compared with control, or a 6% absolute reduction in fracture risk).

RR tends to overestimate fracture risk in some populations and underestimate it in others. [73]

- Compare a 50-year-old woman and an 80-year-old each with a hip T-score of -2.5:
 - They have the same RR for hip fracture (17.6 compared with an age-matched population with normal BMD). [74]
 - But the 10-year probability of hip fracture is much higher in the 80-year-old (19.4%) compared with the 50-year-old (1.9%). [75]
- This is why AR is better than RR for identifying patients most likely to benefit from therapy.

The fracture risk tools, such as FRAX recommended in the latest NOF guidelines, use absolute 10 year risk of fracture, hence their value in communication risk.

9. DECIDING WHO TO TREAT

All patients with low bone density and fracture risk factors should be considered for treatment. [76]

The goal of treating osteoporosis is to prevent fractures and their associated disability.

- Selection of patients for treatment should target those with the highest risk of fracture as defined by low BMD, history of prior fracture, significant secondary causes for developing osteoporosis, and risk factors for falls, such as difficulty with walking or balance. [77]
- Decisions to treat must be made on a case-by-case basis. Guidelines help, but clinical judgment is the deciding factor in treatment decisions. [15]

The benefits of pharmacologic therapy are greater the higher the risk for fracture.

- The Fracture Intervention Trial (FIT) randomized 4,432 with low bone mass (T-score < -1.6) to alendronate or placebo. [78]
 - Over 3 years, alendronate significantly reduced the risk of clinical fractures among women with osteoporosis (T-score < -2.5), but not among women with higher BMD (NNT = 15).
 - Alendronate reduced hip fracture (1.1% vs. 2.2% in the placebo group) and the risk for any clinical fracture (13.6% vs. 18.2%).
 - There was no effect of alendronate on fractures in women with T-scores between -1.6 and -2.5.

The NOF developed a model using the WHO algorithm to determine thresholds for cost-effective therapy in the US population. [79, 80]

- The US-adapted algorithm indicates that pharmacologic therapy is cost-effective for patients with 10-year hip fracture risk of 3% or greater and 20% or greater for any major osteoporotic fracture.

The addition of 1 risk factor (see table below) for patients with BMD of -2.0 increases the 10-year probability for any major osteoporotic fracture above the threshold for treatment in most instances, regardless of racial/ethnic group. [80]

- Although the baseline fracture risk is lower for nonwhite groups, the addition of a risk factor when the BMD was -2.0 increased the 10-year probability risk over the threshold in all age groups.

Ten-Year Probability (%) of Any Major Osteoporotic Fracture: [80]

Age	White Women			
	55 Yrs	65	75	85
Risk factors	No BMD but one risk factor			
None	7.5%	14%	29%	35%
Corticosteroids	12	22	41	44
Rheumatoid arthritis	10	19	38	44
Family history	15	26	39	47
Smoker	7.9	15	30	34
Alcohol	9	17	35	41
Femoral neck T-score	BMD but no risk factors			
1.0	7.5	13	22	22
-1.5	8.8	14	24	25
-2.0	10	16	27	28
-2.5	13	20	32	32

Risk factors	Osteopenia (T-score -2.0) and one risk factor			
Corticosteroids	17	25	39	37
Rheumatoid arthritis	13	21	34	34
Family history	20	30	39	39
Smoker	11	17	27	26
Alcohol	13	19	32	33

Demonstrates the importance of combining T-score with clinical risk factors when determining fracture probability.

- Supports the importance of recognizing the importance of non-modifiable risk factors
- Also, provides evidence to support the benefit of assisting patients to change modifiable risk factors, such as smoking and alcohol consumption.

10. TREATING LOW BONE DENSITY

The treatment of low bone mass includes a combination of nonpharmacologic (lifestyle) and pharmacologic approaches.

- It is critically important for patients to understand that the treatment of osteoporosis will require long-term therapy and strict adherence to the therapeutic regimen prescribed. [76]

NON-PHARMACOLOGIC THERAPY

Evidence clearly suggests that individuals of all ages can do a great deal to promote their own bone health, and health care professionals play a key role in supporting a bone healthy lifestyle. [3]

All patients being considered for treatment of osteoporosis should be counseled on risk factor reduction. [15]

- Patients should be counseled specifically on the importance of calcium, vitamin D and exercise as part of any treatment program for osteoporosis.
- Other interventions to reduce fracture risk include:
 - avoidance of tobacco use,
 - identification and treatment of excessive alcohol use, and
 - treatment of other risk factors for falls, such as impaired vision.

Calcium

Many individuals, especially those at highest risk for osteoporotic fractures, do not obtain adequate calcium and vitamin D. [77]

- National surveys suggest that the average calcium intake is far below levels recommended for optimal bone health. [81]
- Women age 50 and older typically consume only about 600 to 700 mg per day of calcium in their diets. [15]
- Just over half were reported to consume the recommended amount of calcium. [82]

Increasing dietary calcium is the first-line approach, but calcium supplements should be used when an adequate dietary intake cannot be achieved. [15]

- Nonfat and low-fat dairy products are good sources of calcium. Other sources of calcium include dried beans, sardines and broccoli. About 300 mg of calcium are in each of the following: 1 cup of milk or yogurt, 2 cups of broccoli, or 6 to 7 sardines.

The National Osteoporosis Foundation (NOF) supports the National Academy of Sciences (NAS) recommendation that women older than age 50 consume at least 1,200 mg per day of elemental calcium. [15, 83]

- Advise all individuals to obtain at least 1,200 mg per day of calcium, including supplements if necessary.
- Intakes in excess of 1,200 to 1,500 mg per day have limited potential for benefit and may increase the risk of developing kidney stones or cardiovascular disease.

On taking a calcium supplement:

While manufacturers of calcium products proclaim differences in the benefits of different calcium supplements, for most individuals (i.e., with normal intestinal absorption) these differences are not critical.

- By far a lack of dietary calcium intake and non-compliance with calcium supplementation (because of cost, intolerance to the large pill size, etc.) is more commonly the cause of individuals becoming calcium deficient rather than the type of calcium supplement they take.
- Therefore, if individuals do not have sufficient dietary calcium intake, clinicians should advise patients to choose a supplement that they like and will take regularly.

A simple method for estimating the calcium content of a patient's diet: [15]

STEP 1: Estimate calcium intake from calcium-rich foods*

Product	Servings/d [Enter number]	Estimated calcium/ serving, in mg	Calcium, in mg
Milk (8 oz.)	_____ X	300 =	
Yogurt (6 oz.)	_____ X	300 =	
Cheese (1 oz. or 1 cubic in.)	_____ X	200 =	
Fortified foods or juices	_____ X	80 – 1000** =	
TOTAL			

* About 75 to 80 percent of the calcium consumed in American diets is from dairy products.

** Calcium content of fortified foods varies; check label

STEP 2: Total from above + 250 mg for nondairy sources = total dietary calcium

Calcium, in mg: _____

Evidence:

A meta-analysis of randomized controlled trials (RCTs) in which calcium, or calcium in combination with vitamin D, was used to prevent fracture and osteoporotic bone loss (29 trials) found a small but significant 12% reduction in risk of fractures (greater when compliance was high) and a reduced rate of bone loss at the hip and spine. [84]

- The treatment effect was better with calcium doses of about 1200 mg and vitamin D doses of 800 IU or more than lower doses.
- Calcium recommendations vary by age and gender, but all are close to 1200 mg/day. More is not better, as excessive amounts increase the risk of developing renal stones.

Vitamin D

Recognition that vitamin D deficiency may be more prevalent in most patient populations than earlier assumed has resulted in a marked increase in the volume of testing for 25-OH-D in clinical laboratories. [60]

- Currently, there are several laboratory methods in use to assay serum 25(OH) Vitamin D levels. [61] However, there are no established guidelines and no consensus regarding a gold standard assay.
- Until standardization and recommendations are available, clinicians should use the reference ranges provided by the laboratory performing the testing to determine a sufficient level.

Vitamin D plays a key role in the efficient absorption of calcium, bone health, muscle performance, balance and risk of falling. [15]

- NOF recommends an intake of 800 to 1,000 international units (IU) of vitamin D per day for adults age 50 and older. [15]
- This intake will bring the average adult's serum 25(OH)D concentration to the desired level of 30 ng/ml (75 nmol/L) or higher.
- Chief dietary sources of vitamin D include vitamin D-fortified milk (400 IU per quart, although certain products such as soy milk are not supplemented with vitamin D) and cereals (40 to 50 IU per serving), egg yolks, salt-water fish and liver.
- Most calcium supplements and multivitamin tablets also contain vitamin D.

Vitamin D deficiency is an epidemic; 70% of postmenopausal women are vitamin D deficient. Over the age of 70, 90% are vitamin D deficient. [85]

- Patients with malabsorption problems (e.g., celiac disease), chronic renal insufficiency, housebound, chronically ill and others with limited sun exposure are at very high risk of being vitamin D deficient. [83]

Recent evidence suggests that vitamin D intakes above current recommendations may be associated with better health outcomes.

- A review of evidence from studies that evaluated thresholds for serum 25(OH)D concentrations in relation to bone mineral density (BMD) showed that the most advantageous serum concentrations of 25(OH)D are between 90 and 100 nmol/L (36-40 ng/mL). [86]
- An intake of at least 1000 IU of vitamin D daily can optimize serum vitamin D levels in more than half the population.
- The safe upper limit for vitamin D intake for the general adult population was set at 2,000 IU per day in 1997 [83]
- Evidence suggests that, even after prolonged intake of higher doses (10,000 IU), vitamin D toxicity is rare and toxicity does not occur until intake of very large doses (over 20,000 IU). [86a, 86b]

A large body of literature shows that vitamin D has varying effects on fracture prevention, depending on dose, analogs, and population.

- One meta-analysis found that 700 to 800 I.U. daily was necessary to reduce hip and nonvertebral fractures. [87]

The most recent meta-analysis of the anti-fracture efficacy of supplemental vitamin D found that nonvertebral fracture prevention with vitamin D is dose dependent; dosages > 400 IU/day reduced fractures by about 20% in individuals aged 65 years or older. [88]

- Another meta-analysis found that oral vitamin D was more effective when combined with calcium supplementation. [89]

The recommended minimal exposure to sunlight for vitamin D synthesis is about 10 minutes, 3-5 times weekly, of direct sunlight to the face, arms, and/or legs without sunscreen, depending on latitude. [76]

- However, vitamin D studies suggest that it is difficult for all individuals to get sufficient vitamin D from sunlight due to variation in response to UVB. [74]

Regular Weight-Bearing Exercise

Proper exercise may improve physical performance/function, bone mass, muscle strength and balance, as well as reduce the risk of falling. [15]

- Can also improve agility, strength, posture and balance, which may reduce the risk of falls, and may modestly increase bone density.
- But fewer than half (44%) are meeting the minimum recommendation of 30 minutes five times per week. [82]

Although exercise can improve bone density, the main benefit for osteoporosis is the decreased risk of falls due to greater strength to support the body, and improved mobility and balance. [90]

- Although the gains in bone density from exercise are small, complete loss of the ability to bear weight (spinal cord injury, cerebral palsy, wheelchair bound, bedridden) results in rapid and massive declines in bone density (e.g. loss of bone mineral content of 4% per month in areas rich in trabecular bone and 2% per month in areas containing mainly cortical bone. [90a, 90b]
- It has been estimated that a significant portion of this bone loss can be prevented by standing for a minimum of 30 minutes per day.
- Research has not determined what type of exercise is best for osteoporosis or for how long. Until the optimal prescription is determined, most doctors recommend weight-bearing exercise, such as walking, preferably daily. [90]

Evidence:

- There is a lack of RCTs, but a meta-analysis of 13 prospective cohort studies with hip fracture as the end point showed that moderate-to-vigorous physical activity was associated with a 38% reduction in risk of hip fracture. [91]
- A systematic review and meta-analysis of the effects of progressive, high-intensity resistance training on bone mineral density (BMD) in postmenopausal women found a significant consistent increase in BMD of the lumbar spine and femoral neck. Results were better when combined with an increase in calcium intake. [92]

Guidelines: [93]

Before an individual with osteoporosis initiates a new vigorous exercise program, such as running or heavy weight-lifting, a clinician's evaluation is appropriate.

- Provide training for proper mechanics in activities of daily living, including posture, transfers, lifting and ambulation.
- Prescribe assistive devices as needed for improved balance with mobility.
- Implement steps to correct underlying deficits whenever possible, i.e., improve posture and balance and strengthen quadriceps muscle to allow a person to rise unassisted from a chair; promote use of assistive devices to help with ambulation, balance, lifting and reaching.
- Tailor a complete exercise recommendation to the condition of the patient, including:
 - Weight-bearing aerobic activities for the skeleton,
 - Postural training,
 - Progressive resistance training for muscle and bone strengthening,
 - Stretching for tight soft tissues and joints and
 - Balance training.
- Weight-bearing exercise (in which bones and muscles work against gravity as the feet and legs bear the body's weight) includes walking, jogging, Tai-Chi, stair climbing, dancing and tennis.
- Muscle-strengthening exercise includes weight training and other resistive exercises.

As long as principles of safe movement are followed, walking and daily activities, such as housework and gardening, are practical ways to contribute to maintenance of fitness and bone mass.

- Advise patients to avoid forward bending and exercising with trunk in flexion, especially in combination with twisting.
- Avoid long-term immobilization and recommend partial bed rest (with periodic sitting and ambulating) only when required and for the shortest periods possible.
- In patients with acute vertebral fractures or chronic pain after multiple vertebral fractures, the use of trunk orthoses (e.g., back brace, corset, posture training support devices) may provide pain relief by reducing the loads on the fracture sites and aligning the vertebra. However, long-term bracing may lead to muscle weakness and further de-conditioning.

Fall Prevention [15]

The home environment should be evaluated for hazards that increase the possibility of falls.

Major environmental risk factors for falling include:

- Loose throw rugs
- Low level lighting
- Obstacles in the walking path
- Slippery outdoor conditions
- Lack of assistive devices in bathrooms (e.g., wall handles, tub seats, rubber shower mats)

Medical risk factors for falling include:

- Older age
- Anxiety and agitation
- Arrhythmias
- Dehydration
- Depression and cognitive impairment (e.g. dementia)
- Female gender
- Impaired transfer and mobility

- Malnutrition
- Medications (class Ia antiarrhythmics, anticonvulsants, psychotropics, antidepressants, sedatives including benzodiazepines) [15a, 15b]
- Polypharmacy
- Orthostatic hypotension
- Poor vision and use of bifocals
- CNS diseases (stroke, Parkinson's disease, normal pressure hydrocephalus)
- Vestibular dysfunction and hearing impairment
- Proprioceptive disorders (e.g. peripheral neuropathy)
- Musculoskeletal disorders (e.g. arthritis, feet deformities, back deformities)

Strategies to reduce falls include checking and correcting vision and hearing, evaluating any neurological problems, reviewing prescription medications for side effects that may affect balance and providing a checklist for improving safety at home. [15]

- Wearing undergarments with hip pad protectors may protect an individual from injuring the hip in the event of a fall. Hip protectors may be considered for patients who have significant risk factors for falling or for patients who have previously fractured a hip.
- However, evidence suggests that greater benefit is seen in long-term care residents compared to community-dwelling residents who use hip protectors. Poor adherence and incontinence issues may limit widespread application. [93a]

Avoidance of Tobacco Use

Advise patients to avoid tobacco smoking. The use of tobacco products is detrimental to the skeleton as well as to overall health. [15]

- NOF strongly encourages a smoking cessation program as an osteoporosis intervention.

Smoking one pack of cigarettes per day throughout adult life can itself lead to loss of 5% to 10% of bone mass.

- Smoking cigarettes also decreases estrogen levels and can lead to bone loss in women before menopause. Smoking cigarettes can also lead to earlier menopause. In postmenopausal women, smoking is linked with increased risk of osteoporosis. [94]

Avoid Excessive Alcohol Intake

A systematic review and meta-analysis of the associations between alcohol consumption and osteoporosis related outcomes showed that those who consumed from 0.5 to 1.0 drinks per day actually had lower hip fracture risk, but risk increased directly as consumption increased above this level. [95]

- A linear relationship existed between femoral neck bone density and alcohol consumption.

Alcohol intake of three or more drinks per day is detrimental to bone health, increases the risk of osteoporotic fractures, low bone density, and falling and requires treatment when identified. [15]

PHARMACOLOGIC THERAPY

Current FDA-approved pharmacologic options for the prevention and/or treatment of postmenopausal osteoporosis fall into three classes – bisphosphonates, SERMs and hormonal medications. [15]

1. Bisphosphonates: alendronate, alendronate plus D, ibandronate, risedronate, risedronate with 500 mg of calcium carbonate and zoledronic acid
2. SERM (also called estrogen agonist/antagonist): Raloxifene
3. Hormonal medications: calcitonin, estrogen and teriparatide

All these drugs work as anti-resorptive agents, which inhibit osteoclastic activity, except the parathyroid hormone, teriparatide.

- Teriparatide is a potent anabolic agent administered as a daily self-injection that stimulates new bone formation by activating osteoblasts and inhibiting apoptosis in osteoblasts. [97]
- Currently, the FDA limits the use of teriparatide to 2 years due an apparent loss of efficacy after this period of time [97a] and concern regarding a potential risk for osteosarcoma.

- This concern was raised by studies showing high doses of teriparatide administered to rats resulted in the development of malignant osteosarcoma tumors [97b]
- Currently, an increase in incidence of osteosarcoma in humans with 2 years duration of use of teriparatide has not been observed (reference: teriparatide manufacturer, Eli Lilly – 1 in over 750,000 vs. the natural incidence of osteosarcoma (without teriparatide) of 1 in 250,000.)

General approach: [15]

- Bisphosphonates, because of their established efficacy, cost effectiveness and relatively low risk profile, are the first-line of therapy in conjunction with lifestyle changes.
 - Includes a consideration of the differences among bisphosphonate products in terms of onset of action and tolerability, especially GI side-effects, and the differences in mode of administration.
 - Bisphosphonates given by oral administration are poorly absorbed. Therefore, clinicians should advise patients to take first thing in the morning on an empty stomach with plain water and do not eat, drink or take other medications for 30 minutes (60 minutes for oral ibandronate). Due to the risk of GI complications such as esophageal perforation, patients should not lie down for 30 minutes after taking.
- Raloxifene (estrogen agonist/antagonist) has had a limited role, mainly for patients intolerant of bisphosphonate therapy.
 - However, with new concerns about the risk of osteonecrosis of the jaw with long term use of bisphosphonates, some experts suggest that raloxifene is a good choice for younger postmenopausal women who are at low risk for thromboembolic events and cardiovascular disease and may be on antiresorptive medications for many years due to their life expectancy.
- Nasal calcitonin or by self injection is an alternative treatment for patients who have concurrent GI problems or renal insufficiency. Long term studies of the efficacy of calcitonin and head-to-head comparative studies with other bone agents are lacking. Therefore, many experts recommend calcitonin as a second-line medication.
 - Calcitonin has a low risk safety profile and it has a positive analgesic effect in patients with acute vertebral fracture [97c].
- Teriparatide injections are an alternative for severe osteoporosis that should be followed by bisphosphonate therapy to maintain the increase in bone mass produced by teriparatide, however use is limited to no longer than two years.
 - Since studies indicate that prior therapy with a bisphosphonate may blunt the efficacy of teriparatide, ideally, teriparatide therapy should be initiated prior to bisphosphonate use [97d, 97e].
 - However, due to the abundance of bisphosphonate prescribing, in practice teriparatide is commonly used in patients who have been on previous therapies.
 - A recently published review suggests that it may be beneficial to use a short “washout” period of 3-6 months between discontinuing bisphosphonates and initiating teriparatide; it makes clinical sense, but no clinical trials have evaluated the strategy [97f].

Contraindications: [15]

- Oral bisphosphonate therapy -- esophageal stricture or inability to remain upright for at least 30 minutes after administration. Although not a contraindication, caution should be used in patients with gastroesophageal reflux disorder.
- Intravenous bisphosphonate therapy – renal toxicity (decrease in renal function and acute renal failure (rare). Also, contraindicated in patients with hypocalcemia.
- Raloxifene – contraindicated in women with active or past history of venous thromboembolism including deep vein thrombosis, pulmonary embolism, and retinal vein thrombosis and in pregnancy, in women who may become pregnant, and in nursing mothers
- Estrogen
 1. Undiagnosed abnormal genital bleeding.
 2. Known, suspected, or history of cancer of the breast.
 3. Known or suspected estrogen-dependent neoplasia.
 4. Active deep vein thrombosis, pulmonary embolism or a history of these conditions.
 5. Active or recent (within past year) arterial thromboembolic disease (for example, stroke, myocardial infarction).
 6. Liver dysfunction or disease.

- 7. Known or suspected pregnancy
 - Human parathyroid hormone therapy (teriparatide) -- Due to potential risk of osteosarcoma, contraindicated in individuals at risk for osteosarcoma (Paget's disease of bone, prior radiation therapy of the skeleton, bone metastases, or history of skeletal malignancy). In addition, because teriparatide causes a transient increase in serum calcium, patients with hypercalcemia should not receive teriparatide therapy. Since increases in serum calcium may predispose patients to renal stones, caution should be used in patients with a history of renal stones.

Pharmacologic Therapy -- Specific Information: [15]

Alendronate	
Description (Brand name):	A bisphosphonate Brand name: Fosamax® or Fosamax Plus D™. Available as a generic
Approved for:	Prevention and treatment of postmenopausal osteoporosis Treatment of osteoporosis in women taking glucocorticoids.
Administration	Tablets (10 mg daily or 70 mg weekly with or without vitamin D3) taken on empty stomach, first thing in the morning, with 8 ounces of plain water (no other liquid). 35mg weekly tablets are also available (FDA indication for the prevention of osteoporosis in postmenopausal women) Liquid formulation - swallow one bottle (75 ml) and follow with at least 2 oz of plain water. Wait at least 30 minutes before eating, drinking or taking any other medication; remain upright (sitting or standing) during this interval.
Benefits:	Reduces incidence of spine and hip fractures by about 50% over three years in patients with a prior vertebral fracture. Reduces incidence of vertebral fractures by about 48% over three years in patients without a prior vertebral fracture.
Adverse-effects:	GI problems such as difficulty swallowing, inflammation of the esophagus and gastric ulcer, esophageal perforation (rare) and worsening of GERD. Musculoskeletal (bone, muscle or joint) pain. Osteonecrosis of the jaw (rare).
Risedronate	
Description (Brand name):	A bisphosphonate Brand name: Actonel® or Actonel® with Calcium
Approved for:	Prevention and treatment of postmenopausal osteoporosis. Treatment of osteoporosis associated with taking glucocorticoids
Administration	5 mg daily tablet or 35 mg weekly tablet or 35 mg weekly tablet packaged with calcium carbonate; 75 mg tablets on two consecutive days every month or 150 mg monthly tablet Tablets taken on empty stomach, first thing in the morning, with 8 ounces of plain water (no other liquid). Wait at least 30 minutes before eating, drinking or taking any other medication; remain upright (sitting or standing) during this interval.
Benefits:	Reduces incidence of vertebral fractures by about 41-49% and non-vertebral fractures by about 36% over three years.
Adverse-effects:	GI problems such as difficulty swallowing, inflammation of the esophagus and gastric ulcer, esophageal perforation (rare) and worsening of GERD. Musculoskeletal (bone, muscle or joint) pain.. Osteonecrosis of the jaw (rare).

Ibandronate	
Description (Brand name):	A bisphosphonate Brand name: Boniva®.
Approved for:	Treatment of postmenopausal osteoporosis. Oral preparations for prevention of postmenopausal osteoporosis.
Administration	2.5 mg tablets taken on empty stomach, first thing in the morning, with 8 ounces of plain water (no other liquid), followed by at least 60 minutes of remaining upright and not eating, drinking or taking any other medication, OR 150 mg tablet monthly. Also by intravenous injection - 3 mg per 3 ml in prefilled syringe, given over 15 to 30 seconds, once every three months.
Benefits:	Reduces the incidence of vertebral fractures by about 50% over three years.
Adverse-effects:	Oral preparation: GI problems such as difficulty swallowing, inflammation of the esophagus, gastric ulcer, esophageal perforation (rare) and worsening of GERD. Musculoskeletal (bone, muscle or joint) pain.. Osteonecrosis of the jaw.(rare) Intravenous preparation: renal toxicity (decrease in renal function and acute renal failure (rare). Also, contraindicated in patients with hypocalcemia. Osteonecrosis of the jaw (rare) mainly with IV route (mainly in cancer patients)
Other:	Serum creatinine should be checked before each injection (creatinine clearance should be > 30 mL/min).
Zoledronic acid	
Description (Brand name):	A bisphosphonate Brand name: Reclast® and Zometa®.
Approved for:	Treatment of osteoporosis in postmenopausal women; also indicated for the prevention of new clinical fractures in patients who have recently had a low-trauma hip fracture.
Administration	5 mg in 100 ml, is given once yearly by intravenous infusion over at least 15 minutes.
Benefits:	Reduces the incidence of vertebral fractures by about 70% (with significant reduction at one year), hip fractures by about 41% and non-vertebral fractures by about 25% over three years.
Adverse-effects:	Pre-treatment with acetaminophen may reduce risk of acute phase reaction (arthralgia, headache, myalgia, fever) - occurred in 32% of patients after the first dose, 7% after the second dose and 3% after the third dose. Osteonecrosis of the jaw (rare) -- mainly with IV bisphosphonates in cancer patients
Other:	Serum creatinine should be checked before each injection (creatinine clearance should be > 35 mL/min)
Calcitonin	
Description (Brand name):	Salmon calcitonin Brand name: Miacalcin® or Fortical®.
Approved for:	Treatment of osteoporosis in women who are at least five years postmenopausal.
Administration	Delivered as a single daily intranasal spray that provides 200 IU of the drug. Subcutaneous administration by injection also is available.
Benefits:	Reduces the incidence of vertebral fractures by about 40% Positive analgesic effect in patients with acute vertebral fracture
Adverse-effects:	Intranasal form is generally considered safe although some patients experience rhinitis and, rarely, epistaxis.

Estrogen	
Description (Brand name):	Hormone Therapy Brand names: e.g. Climara®, Estrace®, Estraderm®, Estratab®, Ogen®, Ortho-Est®, Premarin®, Vivelle®; HT brand names: e.g. Activella®, Femhrt®, Premphase®, Prempro®.
Approved for:	Prevention of osteoporosis, relief of vasomotor symptoms and vulvovaginal atrophy associated with menopause.
Indications:	Should be used in lowest effective doses for shortest duration to meet treatment goals. When use solely for prevention of osteoporosis, FDA recommends that approved non-estrogen treatments should first be carefully considered.
Benefits:	Woman's Health Initiative (WHI) found that five years of HT (Prempro®) reduced the risk of clinical vertebral fractures and hip fractures by 34% and other osteoporotic fractures by 23%. [21]
Adverse-effects:	Women's Health Initiative (WHI) reported increased risks of myocardial infarction, stroke, invasive breast cancer, pulmonary emboli and deep vein thrombosis during five years of treatment with Prempro®
Raloxifene	
Description (Brand name):	An Estrogen Agonist/Antagonist (formerly SERM) Brand name: Evista®.
Approved for:	Prevention and treatment of osteoporosis in postmenopausal women.
Other Indications:	Reduction in risk of invasive breast cancer in postmenopausal women with osteoporosis.
Benefits:	Reduces risk of vertebral fractures by about 30% in patients with a prior vertebral fracture and by about 55% in patients without a prior vertebral fracture over three years.
Adverse-effects:	Increased risk of deep vein thrombosis similar to estrogen. Increases hot flashes (6% over placebo).
Teriparatide	
Description (Brand name):	Parathyroid Hormone PTH(1-34), An anabolic (bone-building) agent Brand name: Forteo®.
Approved for:	Treatment of osteoporosis in postmenopausal women at high risk for fracture (T-score below -3.0 or a history of fragility fractures).
Administration	Administered by daily subcutaneous injection Safety and efficacy beyond two years unknown, so used for a maximum of two years
Benefits:	Dose of 20 µg daily shown to decrease the risk of vertebral fractures by 65% and non-vertebral fractures by 53% in patients with osteoporosis, after an average of 18 months of therapy.
Adverse-effects:	Well tolerated, although some patients experience leg cramps and dizziness.

National Osteoporosis Foundation. *Clinician's Guide to Prevention and Treatment of Osteoporosis*, 2008. http://www.nof.org/professionals/NOF_Clinicians_Guide.pdf

Summary of FDA-Approved Medications for Osteoporosis

Medication				Postmenopausal Osteoporosis		Glucocorticoid-Induced Osteoporosis	
Generic Name	Brand Name	Dosing Method	Dosing Interval	Prevention	Treatment	Prevention	Treatment
Estrogen	Multiple	Multiple (oral, transdermal, injectable)	Various	✓			
Alendronate	Generic, Fosamax	Pill, liquid	Daily, weekly	✓	✓		✓
Risedronate	Actonel	Pill	Daily, weekly, monthly	✓	✓	✓	✓
Ibandronate	Boniva	Pill	Monthly	✓	✓		
Ibandronate	Boniva	Injection (IV)	3-Monthly		✓		
Zoledronate	Reclast	Injection (IV)	Yearly		✓		
Raloxifene	Evista	Pill	Daily	✓	✓		
Calcitonin	Miacalcin, Fortical	Nasal spray	Daily		✓		
Teriparatide	Forteo	Self-injection (subcutaneous)	Daily (for up to 2 years)		✓		

ePocrates. Computerized pharmacology and prescribing reference. updated daily. Available at: ePocrates.com Accessed September 19, 2008. Micromedex. Available at: micromedex.com.

EVIDENCE SUMMARY

All medications that are approved for treatment of postmenopausal osteoporosis have demonstrated a significant reduction in vertebral fracture risk in randomized, placebo-controlled clinical trials. [87]

- Only the bisphosphonates and estrogen have proven efficacy against hip fractures.
- It should be noted that it is likely, especially in the case of teriparatide, that the other agents also reduce the risk of hip fractures but RCTs to establish efficacy have not been performed. This is because the minimal efficacy required for FDA approval is the prevention of vertebral fractures. Manufacturers are not required to demonstrate efficacy to prevent hip fractures. Furthermore, because hip fractures are rare events compared to vertebral fractures, using hip fracture incidence as a primary outcome requires a very large sample size and/or a long duration of the study (both of which significantly increase the cost of the trial). Therefore, some manufacturers have not, and likely will not, do such studies.

Table. Fracture Risk Reduction in Randomized, Controlled Trials [78, 96, 98-105]

Medication	Spine Fracture Reduction	Nonvertebral Fracture Reduction	Hip Fracture Reduction
Estrogen	X	X	X
Alendronate (Fosamax; Merck and Co, Inc)	X	X	X
Risedronate (Actonel; Procter & Gamble Pharmaceuticals)	X	X	X
Ibandronate (Boniva; Roche Therapeutics Inc)	X		
Zoledronate (Reclast; Novartis)	X	X	X
Calcitonin (Miacalcin; Novartis, Fortical;Upsher-Smith Pharmaceuticals)	X		
Raloxifene (Evista; Eli Lilly)	X		
Teriparatide (Forteo; Eli Lilly)	X	X	

Comparisons of medications [87]

There is limited data from head-to-head trials to compare agents, but what is available suggests that:

- No specific bisphosphonate is superior in preventing fractures.
- Based on limited trial data, bisphosphonates have not been shown to be superior to calcitonin, calcium, or raloxifene in preventing vertebral fractures.
- There is no difference in fracture incidence between bisphosphonates and estrogen.
- There are no RCT data to compare exercise with pharmaceutical agents to prevent vertebral fractures.

A large observational study found little difference in nonvertebral fracture risk for patients taking raloxifene, alendronate, and risedronate. Fracture risk was slightly higher with calcitonin vs alendronate. [106]

POSSIBLE HARMS OF TREATMENT

Bisphosphonates [77]

Gastrointestinal Problems

- Gastrointestinal (GI) problems have been reported with all oral bisphosphonates. Mild upper GI symptoms include acid reflux, esophageal irritation, nausea, vomiting, and heartburn. Serious GI symptoms include esophageal and nonesophageal upper GI perforations, ulcers, and bleeds.

Atrial Fibrillation

- There is concern that bisphosphonates, particularly zoledronic acid, may increase the risk of atrial fibrillation, but the current evidence is conflicting.

Musculoskeletal Pain

- Severe musculoskeletal pain in people taking bisphosphonates is highlighted in a January 2008 Food and Drug Administration (FDA) alert.
- May occur within days, months, or years after drug initiation and require discontinuation. These symptoms are in contrast to an acute response that may accompany initial exposure to bisphosphonates and resolve with continued use.

Osteonecrosis of the Jaw (ONJ)

- ONJ has been associated with both oral and IV bisphosphonates. Most cases have occurred in patients receiving high, frequent doses of IV bisphosphonates for the treatment of hypercalcemia due

to skeletal malignancies, however a few cases have occurred in patients treated with oral bisphosphonates for osteoporosis.

- Currently data are sparse, but some studies suggest that risk factors for ONJ with bisphosphonate use include IV bisphosphonates, cancer and anti-cancer therapy, dental extraction, oral bone manipulating surgery, poor fitting dental appliances, intraoral trauma, duration of exposure to bisphosphonate treatment, glucocorticoids, co-morbid conditions (i.e., malignancy), alcohol and/or tobacco abuse and pre-existing dental or periodontal disease. [101]

SERMs and Hormonal Medications [77]

Stroke

- Estrogen increases the risk of stroke.

Thromboembolic Events

- Raloxifene increases the risk of pulmonary embolism.
- Raloxifene and estrogen increase the risk of venous thromboembolic events.

Breast Cancer

- Estrogen combined with progestin increases the risk of breast cancer.

Gynecologic and Breast Problems

- Estrogen and tamoxifen increase the risk of gynecologic problems, such as endometrial bleeding.
- Estrogen increases the odds of breast abnormalities other than cancer, including pain, tenderness, and fibrocystic changes.

Osteosarcoma

- Based on the results of animal studies with large doses of teriparatide, the FDA warns against prescribing it to those at increased risk for osteosarcoma, such as people with Paget's disease, those having prior radiation therapy of the skeleton, bone metastases, or a history of skeletal malignancy.
- The FDA also recommends against using teriparatide for longer than 2 years.

MONITORING RESPONSE

Patients taking antiresorptive therapy have reduced fracture risk when their BMD increases or at least remains stable. [107]

- This requires having confidence in the precision of serial BMD measurements; every DXA facility must conduct precision assessments using a standardized methodology to know the smallest change in BMD that is statistically significant with a 95% level of confidence.[108]

A significant decrease in BMD should trigger a clinical investigation to identify underlying causes.[109]

- Factors to consider include poor adherence to therapy, malabsorption, inadequate calcium and vitamin D intake, use of medications known to have adverse skeletal effects (eg, glucocorticoids, anticonvulsants), and diseases with adverse skeletal effects (eg, primary hyperparathyroidism, multiple myeloma).

DXA is typically done 1 to 2 years after therapy is started to assess BMD response. [15]

- Once a patient is shown to have the expected effect, then the intervals may be lengthened.
- In patients who are at high risk for rapid bone loss, such as those on systemic glucocorticoid therapy, more frequent BMD measurement (e.g., every 6 months) may be needed. However, prior to ordering more frequent measurements, clinicians should consider if results will alter treatment plans.

Bone turnover markers have a potential role in monitoring therapy, however, there are no established guidelines and the utility of these markers is controversial. [110]

- The absence of suppression of bone turnover in a patient on an antiresorptive medication, or the absence of an elevated bone turnover marker level in a patient on teriparatide, suggests that the medication is not having the expected effect on bone remodeling and further evaluation is needed.
- The advantage of biochemical markers is that they can be measured sooner (e.g., after 3 months) to monitor response, and possibly indicate problems with absorption or compliance.
- Research has shown that a positive response to antiresorptive therapy, as indicated by markers of bone turnover, motivates higher persistence and compliance in patients.

11. COMPLIANCE AND PERSISTENCE

Studies have consistently shown that compliance and persistence with osteoporosis drugs is poor.

- About 50% of patients placed on bisphosphonate therapy are no longer taking these agents at 1 year.[111]
- Others have found the same result - half of women discontinuing treatment within the first year of therapy. [112,113]

Dosing regimens can affect compliance.

- Once-a-week dosing has been shown to be better than daily dosing. [114-119]
- Monthly dosing has also been shown to improve longer term persistence. [119]
- Managed care claims data has shown a 38% reduction in discontinuing therapy with monthly ibandronate vs. weekly alendronate. [120]
- The estrogen agonist/antagonist, raloxifene, and the anabolic agent, teriparatide, both have higher rates of compliance and persistence when compared with bisphosphonates. [121,122]

The results of poor compliance and persistence are well documented.

- Better compliance and persistence means better outcomes; lower compliance and persistence means more fractures.
- Studies of claims data have shown that fracture risk decreased as compliance increased. [123,124] Patients who were refill compliant and persistent had a 20-45% reduction in fracture risk – would translate into roughly 390,000 fractures prevented per year in the US. [125]
- Another managed care database analysis found that low compliance resulted in a 17% increase in fractures and a 37% increase in all- cause hospitalizations. [126]
- Patients who were persistent with bisphosphonate treatment reduced their risk of hospitalization for fractures by 20 to 30%. The protective effect was highest in those who used bisphosphonates consistently for more than one year. [127]

Enhancing compliance and persistence with medication regimens

One method to improve adherence is to include regular contact with a healthcare professional to address patient concerns and educate the patient on the importance of continuing to take the medication.[128,129]

- Another important strategy is to involve the patient as much as possible in decisions regarding dosing options and routes of administration; involving patients in such decisions can increase adherence to the medication regimen over time.[130,131]
- However, with alendronate now available in generic form, many insurers are requiring a trial of generic alendronate (available in only in the weekly dosing regimen) before other oral bisphosphonates (e.g. monthly dosing or non-generic agents) are prescribed.
- In some cases, prior authorization based on medical justification can be provided to override this generic trial, however, patient preference or noncompliance is usually not sufficient.

NOF Strategies to Improving Compliance and Persistence [110]

- Emphasize the value of the treatment regimen
- Emphasize the benefit of compliance and persistence
- Provide simple, clear instructions repeatedly
- Simplify regimen as much as possible
- Listen to the patient and respond to patient preferences
- Positively reinforce desirable behavior with concrete evidence of response to treatment
- Look for markers of non-persistence: missed appointments, lack of response to medication, missed refills
- Elicit patient's feelings about his or her ability to follow the regimen; if necessary, design supports to promote compliance
- Consider role of nurse or other staff in patient monitoring

12. GUIDELINES

SCREENING WOMEN FOR OSTEOPOROSIS

Risk Factor Screening

- There is unanimous agreement that all adult patients should be evaluated for risk factors for osteoporosis at age 50.

Bone Density Screening with DXA - Recommendations

- Screen all women for osteoporosis using DXA at age 65 [consensus of organizations; see table below]
- Screen postmenopausal women under 65 and those in the menopause transition if their risk factor profile suggests increased risk; this requires some clinical judgment
 - NOF, AACE, ACOG, ISCD say this means presence of one risk factor
 - ACPM and OSC say one "major" or two "minor" risk factors

Major risk factors *	Minor risk factors
Vertebral compression fracture	Rheumatoid arthritis
Fragility fracture after age 40	History of hyperthyroidism
Family history of fracture	Chronic anticonvulsant therapy
Systemic glucocorticoid therapy	Low calcium intake
Malabsorption syndrome	Smoking
Primary hypoparathyroidism	Excessive alcohol intake
Propensity to falls	Excessive caffeine intake
Osteopenia on x-ray	Weight < 57 kg (125 lbs)
Hypogonadism	Weight loss > 10% at age 25
Early menopause (< 45)	Chronic heparin therapy

ACPM Position Statement. Am J Prev Med 2009; 36(4): 366-375

* Inability to bear one's body weight, as in paraplegia, is a major risk factor that should be included in the above table.

- Screen all adult women with prior low trauma fractures, or conditions/medications that are associated with low bone mass.

Recommendations of Major Organizations	
USPSTF [1]	<ul style="list-style-type: none"> All ≥ 65 years ≥ 60 years who are at increased risk for osteoporosis (e.g., low body wt, absence of estrogen replacement)
NOF [2]	<ul style="list-style-type: none"> All ≥ 65 years Younger postmenopausal based on clinical risk factor profile In menopausal transition with specific fracture risk factor (e.g., low body wt, prior low trauma fracture, high risk medication) Fracture after age 50 With a condition (e.g., rheumatoid arthritis) or taking a medication (e.g., glucocorticoids, ≥ 5 mg/day for ≥ 3 mos) associated with low bone mass or bone loss Anyone being considered for pharmacologic therapy for osteoporosis
ACPM [3]	<ul style="list-style-type: none"> All ≥ 65 years Younger postmenopausal with at least one major or 2 minor risk factors for osteoporosis
AACE [4]	<ul style="list-style-type: none"> All ≥ 65 years All adults who have history of fracture not caused by severe trauma Younger postmenopausal with clinical risk factors for fracture (e.g., body wt < 127 lbs, family history of hip or spine fracture)

ACOG [5]	<ul style="list-style-type: none"> ▪ All ≥ 65 years ▪ Postmenopausal < 65 who have one or more risk factors for osteoporosis ▪ All postmenopausal with a history of fracture
ISCD [6]	<ul style="list-style-type: none"> ▪ All ≥ 65 years ▪ Postmenopausal < 65 with risk factors for fracture ▪ In menopausal transition with clinical risk factors for fracture (e.g., low body wt, prior low trauma fracture, high risk medication) ▪ All adults fragility fracture, disease or condition or medication use associated with bone loss or low bone mass ▪ Anyone being considered for pharmacologic therapy for osteoporosis
OSC [7]	<ul style="list-style-type: none"> ▪ All postmenopausal > 50 with at least one major or two minor risk factors for osteoporosis
<p>USPSTF = U.S. Preventive Services Task Force NOF = National Osteoporosis Foundation ACPM = American College Preventive Medicine AACE = American Association of Clinical Endocrinologists ACOG = American College Obstetricians and Gynecologists ISCD = International Society for Clinical Densitometry OSC = Osteoporosis Society of Canada</p>	
<p>References:</p> <ol style="list-style-type: none"> 1. Nelson HD, Helfand M, Woolf SH, et al. Screening for postmenopausal osteoporosis: A review of the evidence for the U.S. Preventive Services Task Force. <i>Ann Intern Med</i> 2002;137:529-41. (Available at: http://www.ahrq.gov/clinic/3rduspstf/osteoporosis/osteorr.htm) 2. National Osteoporosis Foundation. <i>Physician's guide to prevention and treatment of osteoporosis</i>. Washington, DC: NOF; 1999. Available at: http://www.nof.org/physguide. 3. Lim L, Hoeksema LJ, Sherin K et al. Screening for osteoporosis in the adult U.S. population. <i>ACPM Position Statement on Preventive Practice. Am J Prev Med</i> 2009; 36(4): 366-375 4. Hodgson SF, Watts NB, Bilezikian JP et al. <i>AACE medical guidelines for clinical practice for the prevention and treatment of postmenopausal osteoporosis: 2001 edition with updates for 2003. Endocrinol Pract</i> 2003; 9: 544-64 5. Neff MJ. <i>ACOG releases guidelines for clinical management of osteoporosis. Am Fam Physician</i> 2004; 69: 1558-60 6. www.iscd.org 7. Brown JP, Josse RC. <i>2002 clinical practice guidelines for the diagnosis and management of osteoporosis in Canada. CMAJ</i> 2002; 167S: S1-34 	

A 2000 Consensus Development Conference sponsored by the U.S. National Institutes of Health recommended an individualized approach to screening, noting that bone density measurement is appropriate when it will aid the patient's decision to institute treatment. [133]

Use of a Risk Assessment Tool

- There is growing consensus recommending the calculation of 10 year fracture risk, based on risk factors and BMD measurement, using the WHO (U.S. modified) FRAX tool. [NOF, ACPM] [15,55]
- The Osteoporosis Self-assessment Tool, is a simple assessment that is also useful for the busy clinician to identify postmenopausal women who would most benefit from BMD testing. [134-136]

MANAGEMENT OF OSTEOPOROSIS

Clinicians should review with patients the relative benefits and harms of available treatment options, and uncertainties about their efficacy and safety, to facilitate an informed choice. [2]

Major Recommendations for Clinicians from the 2008 NOF Guidelines: [15]

Decisions on whom to treat and how to treat are based on clinical judgment, guidelines, and clinical information.

Assessment:

- Detailed patient history pertaining to clinical risk factors for osteoporosis-related fracture.
- Perform physical examination to evaluate for signs of osteoporosis and its secondary causes.
- Assess clinical risk factors for fracture.
- Review potential secondary causes.
- Discuss need for DXA testing if not already done (based on age, risk factors)
- DXA results available: Estimate patient's 10-year probability of hip and any major osteoporosis-related fracture using the US-adapted WHO algorithm.

Explain risk of fracture, the expected course without intervention, and the management options.

Counsel Regarding Non-Pharmacologic Treatment

- Advise adequate amounts of calcium (at least 1200 mg/day) and vitamin D (800-1000 IU/day), including supplements if necessary
- Recommend weight bearing exercise and muscle strengthening exercise to reduce risk of falls and fractures
- Recommend avoiding tobacco smoking and excessive alcohol intake
- Modify risk factors related to falling
- Consider physical and occupational therapy including walking aids and hip pad protectors

Advise FDA -approved medical therapies based on the following:

- Presence of a vertebral or hip fracture
- A DXA hip (femoral neck) or spine T-score ≤ -2.5
- Low bone mass and a US-adapted WHO 10-year probability of a hip fracture $\geq 3\%$ or 10-year probability of any major osteoporosis-related fracture $\geq 20\%$ based on US-adapted WHO absolute fracture risk model (FRAX) – www.nof.org OR www.shef.ac.uk/FRAX
- Consider patient preferences and risk tolerance in the decision to begin pharmacotherapy.

Discuss benefits and risks of each option; explain pros and cons of mode of administration.

- Bisphosphonates (alendronate, ibandronate, risedronate and zoledronic acid)
- Calcitonin
- Estrogen agonist/antagonist (raloxifene)
- Estrogens and/or hormone therapy
- Parathyroid hormone (teriparatide)

Follow-up

- Use BMD DXA testing to monitor bone loss. For patients on pharmacotherapy, it is typically performed 2 yrs after initiating therapy and every 2 yrs thereafter
- If not on medical therapy, re-evaluate when medically appropriate.
- Monitoring plan to assure compliance and persistence with medical therapy (e.g., regular phone calls from nurse to identify problems)

13. ENHANCING PRACTICE PERFORMANCE

The management of a chronic condition, like osteoporosis, requires a partnership between the healthcare team and the patient living with the chronic condition.

- It is something that most practices and reimbursement systems are not set up to provide.
- And, it is perhaps the greatest challenge confronting primary care physicians. [137-140]

Addressing the Compliance Issue

Studies have shown that nurse monitoring and follow up helps to motivate patients to take their medicine as directed. The clinician's staff contacts the patient to schedule a consultation. [110]

- Studies have also shown the effectiveness of patient education in improving medication compliance and persistence. [141]
- Carving out the time to counsel patients poses a challenge. Modest improvements in compliance and persistence have been observed with the use of videotaped patient education instruction, but have not found written materials in the absence of counseling to be effective. [141]
- The best improvements in compliance and persistence for patients with chronic diseases like osteoporosis appear to come with repeated face-to-face educational interventions provided by clinicians or knowledgeable healthcare support staff. [142]
- The 2004 Surgeon General's report on bone health and osteoporosis stated: "Nurse practitioners, nurse midwives and physician assistants can contribute significantly to the provision of bone health care. They can educate patients...and monitor compliance with treatment." [3]

Using a Case Manger Approach

An intervention that used an osteoporosis case manager to educate patients, arrange bone mineral density tests, provide prescriptions, and communicate with primary care physicians was compared with usual care in a RCT. [40]

- Six months after hip fracture, 51% of the intervention group were receiving bisphosphonate therapy compared with 22% in the usual care group. BMD tests were performed in 80% of the intervention group vs 29% of the control group. Patients in the intervention group were more likely to receive appropriate care than were patients in the control group (67% vs 26%).

The Chronic Care Model

The Chronic Care Model [144] recognizes the changes needed to organize health services for people with chronic conditions, and offers a guide for improving practice performance. The model has been endorsed by the AAFP, along with health care organizations all over the world. [145]

- It emphasizes office redesign and the use of nonphysician staff to accomplish disease management tasks. [146-149]
- The goal of the model is the development of prepared, proactive teams that prepare and partner with informed, activated patients.
- Due to time constraints, physicians have no choice but to create teams, either within the practice or using community resources, along with well written educational materials to help patients modify certain behaviors.

The model focuses on improving performance in six interrelated components: [145,150]

- 1) Self management support – the key to effective chronic care
 - To assist patients in becoming better informed and activated self managers
 - Includes providing encouragement and information, teaching specific skills, promoting healthy behaviors, teaching problem solving skills, assisting with emotional support, maintaining regular and sustained follow-up
- 2) Practice re-design – two elements required to provide self management support:
 - Planned visits – using a pre-determined agenda; can include individual or group visits, phone calls or emails, internet programs
 - Care teams – identify roles, provide needed training; includes clinicians, nurses, dietitians, social workers, behavioral health professionals, health coaches, exercise therapists, community health workers

- 3) Decision support -- using evidence-based recommendations and guidelines
 - Chart reminders for recommended services and
 - Electronic record protocols for referrals to specialists
- 4) Clinical Information Systems – to track care
 - Develop registry – patient list with preventive and chronic care needs and relevant clinical information
 - Team member designated to periodically review, update, identify needed services, reminders to send out
 - Separate registries can be created for patients with the Metabolic Syndrome, or other chronic conditions, or other specific criteria
- 5) Health care organization – two key elements required to redesign the practice:
 - Leadership – understand and embrace the Chronic Care Model
 - Financing – comprehensive per-patient payments rather than fee for service financing, which usually does not reimburse ancillary services
- 6) Community Resources
 - Primary care practices can rarely provide all of the services needed for patients with chronic conditions – need to know and encompass local resources to fill the gaps in promoting healthy lifestyles

A practical way to pay for and target chronic care activities is to reimburse physicians for units of service delivered by their team. California's well-established Comprehensive Perinatal Services Program (CPSP) is a good example of a payment mechanism that supports health education and case management services through payments to physician employers. [151,152]

- The Future of Family Medicine report predicted that implementation of the Chronic Care Model would have a positive impact on office costs after making assumptions regarding time required and reimbursement for providing high-quality care. [153]

14. RESOURCES

GUIDELINES:

NOF:

National Osteoporosis Foundation. Clinician's Guide to Prevention and Treatment of Osteoporosis, 2008.

http://www.nof.org/professionals/NOF_Clinicians_Guide.pdf

AHRQ:

AHRQ. Fracture Prevention Treatments for Postmenopausal Women with Osteoporosis. *Clinician Summary Guide, 2008*; AHRQ Pub. No. 08-EHC008-3

<http://effectivehealthcare.ahrq.gov/repFiles/LowBoneDensityClinician.pdf>

AACE:

American Association of Clinical Endocrinologists medical guidelines for clinical practice for the prevention and treatment of postmenopausal osteoporosis. *Endocrine Practice* 2003;9:545-564.

POSITIONS AND REPORTS:

ACPM:

Lim LS, Hoeksema LJ, Sherin K; ACPM Prevention Practice Committee. Screening for osteoporosis in the adult U.S. population: ACPM position statement on preventive practice. *Am J Prev Med.* 2009 Apr;36(4):366-75.

USPSTF:

Nelson HD, Helfand M, Woolf SH, Allen JD. Screening for postmenopausal osteoporosis: a review of the evidence for the U.S. Preventive Services Task Force. *Annals of Internal Medicine* 2002;137:529-541 and 526-528. www.ahrq.gov/clinic/3rduspstf/osteoporosis/osteorr.htm

NAMS:

Management of osteoporosis in postmenopausal women: position statement of The North American Menopause Society, [Menopause 2006;13:340-367](http://menopause.2006.13.340-367).

ACR:

American College of Rheumatology ad hoc Committee on Glucocorticoid-induced Osteoporosis. Recommendations for the prevention and treatment of glucocorticoid-induced osteoporosis. 2001 update. *Arthritis and Rheumatism* 2001;44:1496-1503.

SURGEON GENERAL:

Bone Health and Osteoporosis: A Report of the Surgeon General, Issued October 14, 2004
<http://www.surgeongeneral.gov/library/bonehealth/index.html>

RISK ASSESSMENT TOOLS:

WHO Fracture Risk Assessment Tool [FRAX]

<http://www.shef.ac.uk/FRAX/>

- Estimates 10 year fracture risk based on nationality, age, gender, height, weight, previous fractures, parental history of hip fracture, current smoking status, use of glucocorticoids, presence of rheumatoid arthritis, excessive alcohol use (> 3 units/day), secondary osteoporosis, femoral neck BMD

The NEW IOF One-Minute Osteoporosis Risk Test

<http://www.iofbonehealth.org/patients-public/risk-test.html>

Osteoporosis Self Assessment Tool

http://www.menopauserx.com/health_center/assessment_osteo.htm

Table of Calcium-Rich Foods

<http://www.iofbonehealth.org/patients-public/about-osteoporosis/prevention/nutrition/calcium-rich-foods.html>

Bone Health ratio of Calcium to Magnesium

<http://www.spineuniverse.com/displayarticle.php/article1080.html>

ORGANIZATIONS (General Info):

National Osteoporosis Foundation (NOF)

1232 22nd Street, NW, Washington, DC 20037

Phone: (202) 223-2226 • Fax: (202) 223-2237

<http://www.nof.org/>

- NOF can provide a free packet of information for health fairs that includes 50 brochures as well as handouts to copy and give out. Call NOF toll-free at (800) 231-4222 to request this packet of materials for your next health fair or community event.
- NOF has free educational materials on many osteoporosis topics. Patients can call toll free at (800) 231-4222 to request this free information.
- NOF also provides all the educational materials and other resources to help you launch a support group and conduct meetings. It benefits patients and extends the reach of your practice in the community.
- For information, call the NOF support group coordinator toll free at (800) 231-4222.
- To help people connect with others who have osteoporosis, NOF has launched an online health community. Participation is open to people concerned about their bone health, patients with osteoporosis, caregivers, family members and healthcare professionals.
- Join NOF's online health community at: <http://nof.inspire.com/>

International Society for Clinical Densitometry (ISCD)

<http://www.iscd.org/>

International Osteoporosis Foundation (IOF)

<http://www.iofbonehealth.org/>

CME:

AMA Online Series Osteoporosis Management

http://www.ama-cmeonline.com/osteo_mgmt/index.htm

GENERAL INFORMATION:

The NIH Osteoporosis and Related Bone Diseases ~ National Resource Center

http://www.niams.nih.gov/Health_Info/bone/default.asp

Lots of links

<http://www.nlm.nih.gov/medlineplus/osteoporosis.html>

Overview from NIH

http://www.niams.nih.gov/Health_Info/Bone/Osteoporosis/default.asp

FOR PATIENTS:

From the AHRQ:

Osteoporosis Treatments That Help Prevent Broken Bones: A Guide for Women After Menopause

- Companion to Clinician's Guide to help women talk with health care professional about treatment options.

<http://effectivehealthcare.ahrq.gov/healthInfo.cfm?infotype=sg&DocID=92&ProcessID=8>

American Academy of Family Physicians:

Osteoporosis in Women: Keeping Your Bones Healthy and Strong

<http://familydoctor.org/online/famdocen/home/seniors/common-older/136.printerview.html>

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