Osteoporosis: Diagnosis and Management

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Faculty Disclosure

Contributing faculty, John J. Whyte, MD, MPH, has disclosed no relevant financial relationship with any product manufacturer or service provider mentioned.

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Audience

This course is designed for dental professionals, especially those working with patients who present with suspected osteoporosis.

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Course Objective

To appropriately prevent, diagnose, and treat osteoporosis, clinicians should understand the epidemiology, physiology, and management. The purpose of this course is to provide dental professionals with the information regarding causes and treatment of osteoporosis necessary to effectively provide patient-centered care.

Learning Objectives

Upon completion of this course, you should be able to:

1. Discuss the clinical background of osteoporosis, noting the various definitions used in the past few years.
2. Discuss the epidemiology of osteoporosis in the United States, based on age, sex, race, and other factors.
3. Identify the primary and secondary causes of osteoporosis.
4. Identify the various risk factors for osteoporosis.
5. Describe the signs and symptoms of osteoporosis.
6. List the various screening recommendations established for osteoporosis.
7. Explain the various treatment modalities for osteoporosis.
8. Describe the current dietary and physical activity recommendations related to osteoporosis.
9. Discuss the pharmacologic treatment of osteoporosis, including indications and adverse reactions and the importance of utilizing interpreters in providing care to non-English-proficient patients.

Sections marked with this symbol include evidence-based practice recommendations. The level of evidence and/or strength of recommendation, as provided by the evidence-based source, are also included so you may determine the validity or relevance of the information. These sections may be used in conjunction with the course material for better application to your daily practice.

INTRODUCTION

Osteoporosis has increasingly become a major health problem. The Bone Health and Osteoporosis Foundation (BHOF) (formerly the National Osteoporosis Foundation) has estimated that 10 million Americans have osteoporosis and 44 million have low bone mass, or osteopenia, which places them at risk for osteoporosis [1; 2]. Approximately 1 in 2 women and 1 in 4 men 50 years of age and older will have an osteoporosis-related fracture in their lifetime [3].

Osteoporosis is the most common type of metabolic bone disease. It results either from the body's inability to form new bone or from an increased resorption of formed bone. Essentially, when there is an imbalance between osteoblastic and osteoclastic activity, skeletal problems arise. Risk factors, such as advanced age, family history, race, estrogen deficiency, tobacco use, steroid use, low calcium intake, physical inactivity, and low body weight, contribute to this condition [4].

Several diagnostic techniques have improved the ability to diagnose osteoporosis, most notably dual-energy x-ray absorptiometry (DXA), which is considered the gold standard for diagnosing osteopenia or osteoporosis [5]. Ultrasound, radionuclide absorptiometry, quantitative computed tomography (CT), and magnetic resonance imaging (MRI) also have been used to assess risk of fracture [6]. In the United States, current diagnostic criteria are based solely on quantitative CT hip and DXA spine or hip T-score measurements [7; 8]. Along with these diagnostic techniques, biochemical markers, such as hydroxyproline and collagen cross links, may be used to identify patients at risk [5; 9]. Several screening guidelines have been published indicating the preferred techniques and indications.

Treatment of osteoporosis remains controversial. The focus of management has been on slowing or stopping bone loss or creating new bone. Because of the significant disability, morbidity, mortality, and costs associated with osteoporosis-related fractures, the American College of Physicians recommends that treatment be aimed at fracture prevention [10]. First-line therapy remains diet supplementation and regular weight-bearing and muscle-strengthening exercises, both of which should be started before 30 years of age [11; 12]. Numerous medications, either antiresorptives or bone formation agents (anabolics), exist with different patient indications, adverse events, and contraindications. Additionally, several high-profile studies have impacted the treatment and prevention of osteoporosis. Specifically, the Heart and Estrogen/Progestin Replacement Study (HERS) and the Women's Health Initiative (WHI) have indicated some potential dangers (e.g., increased risk of breast cancer, heart attack, stroke, blood clots in the legs and lungs) associated with estrogen replacement, which until recently had been one of the mainstays of treatment [13; 14].

To effectively prevent, diagnose, and treat this disease, physicians and other healthcare providers should understand the epidemiology, physiology, and management of osteoporosis. The following case study will be referenced throughout the text to illustrate the challenges of treating patients with osteoporosis.

An Asian woman, Patient D, is 64 years of age with a history of type 2 diabetes, asthma, hypertension, and degenerative joint disease. She presents to a general medicine clinic with persistent lower back pain. The patient reports that for the last few months, she has been experiencing aching pain in the lower lumbar area. It is worse with exertion. The pain is fairly localized, without radiation. She does not experience any tingling, numbness, or weakness. There is no history of trauma. On exam, blood pressure is 135/75 mm Hg, heart rate 72 beats per minute, respirations 18 breaths per minute, temperature 99 degrees Fahrenheit, height 59 inches (150 cm), and weight 99 lbs (45 kg).

The patient does exhibit some tenderness to palpation in the lower lumbar area. She notes that she tries to remain active, walking about 2 to 3 miles, three or four days a week; she is also a devoted gardener. She is concerned enough about this pain that she believes she needs an x-ray. She also reluctantly remarks that she is not sure if she is exaggerating, but she feels she might be "shrinking." She recently tried on a pair of pants she purchased several years ago, and now they appear to be too long. She wants to know if this is possible. One of her sisters recently told her that she was diagnosed with "brittle bones." She asks you what this means and if she should be concerned.

DEFINITIONS

The definition of osteoporosis has evolved over the past few decades. Osteoporosis has been described colloquially as "thin bones" or "brittle bones," and at one time, the diagnosis of osteoporosis relied on the occurrence of a low-trauma fracture. The most widely accepted medical definition was proposed in 1991 and reaffirmed in 1993 at consensus development conferences supported by the National Institute of Arthritis and Musculoskeletal Disease of the National Institutes of Health and the BHOF. At those conferences, osteoporosis was defined as [15; 16]:

> A systemic skeletal disease characterized by low bone mass and microarchitectural deterioration of bone tissue, leading to enhanced bone fragility and a consequent increase in fracture risk.

In 1994, a World Health Organization (WHO) working group determined a level of bone mineral density (BMD) that would be clinically applicable and consistent with the new definition [17]. This was due to a desire to seek a more quantitative, rather than qualitative, definition. Additionally, this group published a set of standards to define the patient with osteopenia. Osteopenia had been loosely defined as low bone mass or decreased calcification of bone without the clinically increased risk of fracture. However, there is a wide spectrum of bone quality and strength. Frequently, osteopenia is a precursor of osteoporosis.

T-SCORE

A T-score is the quantitative measurement of bone mineral density obtained by an examination, such as DXA, of the hip or other acceptable skeletal region. The score is the number of standard deviations from the mean (average) bone density for a young healthy adult. The exact age range used varies among authorities, but it is usually from 20 to 30 years of age.

Z-SCORE

Similarly, a Z-score is the number of standard deviations from the mean bone density for age-matched, sex-matched, and ethnicity-matched patients. For example, a woman 75 years of age with a Z-score of -1.0 is one standard deviation below the BMD of average women 75 years of age, but her T-score may be -3.0 because she is 3 standard deviations below the BMD of an average woman 30 years of age. Alternatively, an elderly patient's T-score may be low, but average for her age by Z-score. For a young adult woman, the T-score and Z-score should be the same.

For each standard deviation decrease in BMD, there is a doubling of fracture risk [18]. A patient with a T-score of -1.0 is twice as likely to sustain a fracture as someone with a T-score of zero; a patient with a T-score of -2.0 indicates a fourfold increase in risk of fracture, and so on. The WHO working group determined that patients with T-scores of at least -2.5, or 2.5 standard deviations below the young healthy mean, would meet the diagnostic criteria for osteoporosis. Those with T-scores from -1.0 to -2.5 would fall into the range for osteopenia (***Table 1***). Statistically, a cutoff of one standard deviation below the mean would categorize roughly 24% of all women with osteopenia and around 1% with osteoporosis. (Note that these statistics assume a normal distribution of data.)

WHO CRITERIA FOR DIAGNOSIS OF OSTEOPOROSIS BY T-SCORE	
T-Score	**Diagnosis**
Equal to or above -1	Normal range
Between -1 and -2.5	Osteopenia
Equal to or below -2.5	Osteoporosis
Equal to or below -2.5 + fracture	Severe osteoporosis

Source: [19; 20] *Table 1*

The WHO criteria are easy to use for study inclusion criteria as well as epidemiologic data; however, individual patient decisions should not be based solely on a T- or Z-score. Just as total cholesterol is not the only risk indicator for coronary events, single quantitative measurements, like a T- or Z-score, must be combined with individual patient characteristics to make clinical decisions. Bone mineral density may account for 70% of bone strength; however, bone quality, the rate of bone turnover, and other architectural properties of bone (as well as genetics) play an important role in the development of osteoporosis and bone fragility [5; 21].

Although the WHO definition includes measurement of bone density at several possible sites, such as the spine, heel, or wrist, BMD measured at the hip, femoral neck, and lumbar spine is preferred by most authorities. There are slight variations in the degree of fracture risk with BMD measurements at the different sites (e.g., T-score at the hip correlates to greater fracture risk than the same T-score taken at the spine). If measurements are made at different sites, fracture risk is determined according to the lowest values obtained. It must be emphasized that the WHO BMD T-score diagnostic classification should be used with caution in men and children because established criteria are primarily based on an adult female population. The diagnosis of osteoporosis in these groups should not be made based on densitometric criteria alone; the International Society for Clinical Densitometry (ISCD) has recommended instead that ethnicity- or race-adjusted Z-scores be used [20].

EPIDEMIOLOGY

As noted, an estimated 10 million individuals in the United States already have osteoporosis, and another 44 million have low bone density [1; 2]. According to data from the BHOF, 8.2 million American women 50 years of age and older have osteoporosis and 27.3 million are at risk of developing the disease [22]. The diagnosis of osteoporosis is important as a predictor of fracture. Osteoporosis results in more than 2 million osteoporotic fractures every year. This number is expected to double or triple by 2040 [23]. To fully understand the epidemiology of osteoporosis, one must examine the effects of race, gender, and age.

ETHNICITY/GENDER

Women are the most commonly affected population in the United States due to a lower peak bone mass and an accelerated bone loss in the postmenopausal period [3]. Osteoporosis is under-recognized and undertreated in African American women and is increasing most rapidly among Hispanic women [3; 5]. White and Asian women are at highest risk for osteoporotic fracture; African American and Hispanic women have a lower but significant risk [3; 5]. The National Osteoporosis Risk Assessment (NORA) study found that the fracture rates in postmenopausal Hispanic, African American, and Asian women were 91%, 54%, and 41%, respectively, of the fracture rates in white women [24].

Men also are affected by osteoporosis, although they represent only about 20% of the cases [5]. Part of the reason for this may be that this population has not been studied as frequently as postmenopausal women. In fact, the number of men with osteoporosis has not been clearly quantified, and the WHO bone mineral density cut-offs are not necessarily applicable. In general, men have greater peak bone mass and greater BMD [3]. As a result, they usually present with fractures 10 years later than women [25]. Sex-specific T-scores are available, but the appropriate cut-offs have not been definitively determined; more research is needed. Up to 20% of hip fractures and 20% of vertebral fractures occur in men. Of note, mortality associated with hip fractures in men is nearly 50% higher than in women [5; 25].

AGE

All patients lose bone mass as they age. Consequently, the incidence of osteoporosis increases with age. Age does predict fracture risk independent of BMD; however, osteoporosis is not an inevitable consequence of aging [11]. For patients with the same T-score, there is still a significant difference in fracture risk across age groups. For example, a woman 80 years of age with a T-score of -2.0 has a greater risk of hip fracture over 10 years than does a woman 70 years of age with the same T-score. This difference is likely attributable to decreasing bone quality as well as other factors, including unsteadiness, decreasing muscle strength, and comorbidities that occur with aging [24].

COSTS

Osteoporotic fractures account for an estimated $19 billion in healthcare expenditures annually [2]. These costs are expected to rise to $25.3 billion by 2025 [2]. Osteoporosis causes nearly 300,000 hip fractures, 547,000 vertebral (spine) fractures, 397,000 wrist fractures, and almost 675,000 other fractures each year. Annual medical costs related to hip fractures alone are expected to double or triple by 2040 [26]. Osteoporosis results in more than 432,000 hospital admissions, 2.5 million physician visits, and 180,000 nursing home admissions annually [20]. Notably, statistics relating to cost are most often based on treatment and hospital costs, thereby underestimating the true total costs associated with this disease [27].

The indirect costs of osteoporosis have not yet been accurately ascertained, but the decreased productivity, lost wages, and psychologic and social factors associated with osteoporosis and related fractures are substantial. For example, hip fracture patients have demonstrated a lower baseline health-related quality of life and a prolonged and significant deterioration in health-related quality of life following hip fracture [28; 29].

The costs of osteoporosis should also encompass the effects on people around the patient. The caregiver and close family members also suffer decreased productivity due to the emotional and physical strain associated with the high level of care required for these patients.

PATHOPHYSIOLOGY

The development of osteoporosis results from defective bone remodeling. Normally, bone is under a continuous remodeling process of formation by osteoblasts and resorption by osteoclasts. When the resorption exceeds the formation (either due to decreased formation, increased resorption, or combination of the two), bone density decreases, bone quality deteriorates, and the patient develops osteopenia or osteoporosis.

Osteoblasts are formed from the same precursors as fibroblasts, the cells that produce collagen. They ultimately are responsible for the formation of osteoid, or bone matrix. Mineralization of this osteoid matrix produces bone, and the osteoblasts that remain following mineralization become the osteocytes, the functioning bone cells. Osteoblasts respond to a variety of humoral factors, such as estrogen, vitamin D, cytokines, and the various growth factors that stimulate bone formation.

Osteoclasts act in opposition to osteoblasts and, interestingly, result from a line of hematopoietic cells. Like osteoblasts, they respond to many signals that are necessary for cell development. Because osteoclasts are formed from the same line as many blood cells, they also respond to granulocyte colony-stimulating factor and a wide range of interleukins. They are inhibited in their differentiation by the protein osteoprotegerin. Osteoclasts attach to endosteal bone and secrete acid to dissolve calcium crystals. Enzymes like metalloproteinases then act to break down the protein matrix and the osteoclast undergoes apoptosis. The breakdown materials from this protein degradation may be measured as possible markers of bone resorption.

The imbalance of osteoclastic and osteoblastic activity may be caused by several age- and disease-related factors. There is some difference of opinion about how to classify the categories of osteoporosis; however, many authorities utilize three main categories: primary osteoporosis, postmenopausal osteoporosis (generally included in the category of primary osteoporosis), and secondary osteoporosis [23].

PRIMARY OSTEOPOROSIS

Primary, age-related, or low-turnover osteoporosis results from decreasing bone mineral density and bone quality with age. Normal aging processes decrease gonadal function, and physical activity is usually less strenuous. Everyone reaches a peak bone mass around the third decade of life, usually between 25 to 30 years of age. The maximum BMD achieved by any individual depends upon genetic factors, nutrition, endocrine status, and physical activity. Bone density then gradually decreases as the individual ages. This primary type of osteoporosis is due to decreased bone formation without declining osteoclastic action. The molecular changes that lead to this type of osteoporosis are not clear at this time; however, micrographs of bone show loss of trabecular plates in cancellous bone [20].

POSTMENOPAUSAL OSTEOPOROSIS

Postmenopausal osteoporosis causes most of the skeletal difficulties in the adult female population. Again, these molecular processes are not well understood. It is known that declining estrogen levels cause an increase in osteoclastic activity with a resulting imbalance between skeletal formation and resorption [23]. Estrogens act on nuclear receptors of both osteoblasts and osteoclasts. Deficiency of estrogen leads to, among other effects, the upregulation of osteoprotegerin ligand gene transcription and increased production of macrophage colony stimulating factor (M-CSF), both of which result in increased osteoclastic activity [30].

SECONDARY OSTEOPOROSIS

The final category is osteoporosis due to secondary causes. This can be from many diseases, including liver disease, rheumatoid arthritis, celiac sprue or other malabsorption syndromes, inflammatory bowel disease, lymphoma, multiple myeloma, thalassemia, acromegaly, amyloidosis, leukemia, and thyrotoxicosis. Nutritional deficiencies or medications that have effects on calcium, sex steroids, or other factors related to bone formation or resorption also may cause secondary osteoporosis [23]. In men, 30% to 60% of osteoporosis cases have been associated with secondary causes [25]. In perimenopausal women, about half of the cases are due to secondary causes, such as hyperthyroidism and anticonvulsant treatment. The most common medications associated with osteoporosis are glucocorticoids. Even small doses (i.e., 2.5–7.5 mg prednisone per day) have been associated with an increase in fractures [23]. Patients with osteoporosis should have possible secondary causes explored, as many of the conditions are treatable.

RISK FACTORS

There are numerous risk factors that predict low BMD, the development of osteoporosis, and resulting fractures. Risk factors include advanced age, white race, tobacco use, female gender, low body weight, physical inactivity, and others (***Table 2***). Each risk factor has a different impact on the development of osteoporosis.

When evaluating risk factors, it is important to discuss with patients those risk factors that they can modify. Some modifiable risk factors directly impact bone biology and result in a decrease in BMD. Others increase the risk of fracture independently of their effect on bone [31]. For example, smoking is well correlated with an increase in postmenopausal bone loss and fracture risk [21; 31]. Alcohol use is also a consistent risk factor for osteoporosis and fracture, though its effects seem to be dose-related. Drinking some but less than one drink a day may be protective, perhaps because of an effect on estrogen, but larger amounts of alcohol (i.e., two or more drinks/day) increase the risk of osteoporosis and fracture by 40% [20; 31]. High caffeine intake also may increase the risk of fracture in older women [20].

Low physical activity is also an important risk factor that should be modified. Exercise is important for maintaining strong bones, physical ability, and independence throughout life and, depending on the individual's age, may increase or preserve bone mass and help reduce the risk of falls and fractures [23]. Patients with nutritional deficiencies of calcium and vitamin D also are at increased risk of osteoporosis. Protein may also be important due to its synergistic action with vitamin D and calcium [31]. Building a maximal peak bone mass as a child and adolescent is very important, and continuing to receive adequate amounts of these nutrients also is necessary.

RISK FACTORS FOR OSTEOPOROSIS
Advanced age
Low body weight (<70 kg)
Family history
Low physical activity
White race
Medications
Female gender
Menopause/hysterectomy
Tobacco use
Previous fracture
Low cognitive function
Estrogen deficiency
Low calcium intake
Source: Compiled by Author — *Table 2*

Clinicians and patients should be aware of medications that may increase the risk of osteoporosis. As noted earlier, glucocorticoids are the most common cause. The list of medications that may increase the risk of osteoporosis includes [20; 23]:

- Anticonvulsants
- Anticoagulants (long-term use)
- Thyroxine
- Lithium
- Tamoxifen (premenopausal use)
- Immunosuppressants and cytotoxic drugs

Many of these drugs have different mechanisms of action. For instance, some of the anticonvulsants (e.g., phenytoin, phenobarbital) increase hepatic metabolism of vitamin D, resulting in decreased calcium absorption in the intestine. The key is to be aware of these medications and their impact on osteoporosis.

Patient D has numerous risk factors for osteoporosis, including older age, female gender, and low body weight. She may also have a family history, and this should be explored further. Upon review of her medications, she has been treated with steroids for exacerbation of asthma, but there have been no such episodes in the past year. In addition, she is not on estrogen replacement therapy. The use of steroids and estrogen deficiency may be additional risk factors. Her level of physical activity is encouraging, but it does not offset her numerous risk factors.

PREVENTION

Although the process of bone thinning is a natural part of aging and cannot be completely stopped, there are measures that can and should be taken early to prevent or delay osteoporosis. Ideally, it is best to start these measures during adolescence; however, adults who follow them also may benefit. An estimated 10% increase of peak bone mass in children reduces the risk of osteoporotic fracture during adult life by 50% [31]. Preventive measures include [20; 23; 31]:

- A balanced, nutritious diet rich in calcium and vitamin D
- Maintenance of a healthy body weight
- Beneficial weight-bearing exercise for 30 to 60 minutes, five days a week
- No use of tobacco products and only moderate (if any) alcohol consumption, and avoid secondhand smoke, if possible
- Fall prevention
- Careful medication usage, recognizing which agents increase risk for osteoporosis, and seeking alternatives, if possible

The American Association of Clinical Endocrinologists recommends counseling patients to maintain adequate dietary intake of calcium, to a total intake (including diet plus supplement, if needed) of 1,200 mg/day for women 50 years of age or older.

(https://www.sciencedirect.com/science/article/pii/S1530891X20428277. Last accessed October 15, 2024.)

Level of Evidence: Grade B (Evidence from at least one well-designed clinical trial, cohort- or case-controlled analytic study, or meta-analysis)

Falls often precipitate fractures in individuals with low BMD. They occur for a variety of reasons and may involve multiple factors (e.g., problems with balance, mobility, vision, lower extremity weakness, and/or blood pressure circulation). Falls are a major contributor to hip fractures and have also been associated with an increased risk of spine, wrist, pelvis, and upper arm fractures. Preventive measures should include regular vision checks, elimination of medications that may cause dizziness, low blood pressure, or confusion, and elimination of environmental obstacles (e.g., removing throw rugs, installing night lights). Another important fall prevention measure is physical activity, which may help to improve muscle strength and balance. Physical activity, performed an average of three times each week for a duration of 30 to 45 minutes, should be encouraged in the elderly [23].

Both smoking and heavy alcohol consumption have been associated with reduced bone mass and increased fracture risk. Smoking has been found to have a direct toxic effect on bone cells and may also harm bone indirectly by lowering the amount of calcium the intestine is able to absorb [23]. Heavy alcohol consumption has known negative effects on bone and bone remodeling [23].

Healthcare providers should review these preventive measures frequently with patients and be certain that language or cultural differences do not interfere with the patient's ability to understand them.

DIAGNOSIS

CLINICAL SIGNS AND SYMPTOMS

Osteoporosis is often a silent disease without obvious indications that it is present. However, there are some signs and symptoms that may accompany the development of the condition, including [23; 32]:

- Decreasing height (patients may lose 10–15 cm in height due to collapsing vertebrae)
- Back pain (typically in the lower thoracic and lumbar areas, T5–L5)
- Development of a kyphosis or curvature of the upper back (Dowager hump)
- Fracture occurring with minimal trauma
- Low body weight and weight loss of more than 1% per year in the elderly
- Suspicion of vitamin D deficiency (e.g., due to low intake or little exposure to sunshine)

Any of these findings in a patient should lead to an evaluation for osteoporosis. A fracture in at-risk populations, especially one that is disproportionate to the amount of trauma, should prompt a work-up. Subtle vertebral fractures may be identified incidentally on chest radiographs or bone scans. A vertebral fracture assessment (VFA) may be needed if a vertebral fracture is suspected in certain populations [33]. Acute onset of low back pain with little or no trauma could represent a vertebral compression fracture. Wrist fractures (either Smith or Colles) should raise suspicion in a younger population; they often are an earlier manifestation of osteoporosis, with increasing incidence in women 40 years of age and older [34].

As noted, most often patients do not present with significant signs or symptoms of osteoporosis. In this example, Patient D does present with back pain in the lower lumbar area, which has been persistent for several months. The physical exam does not reveal any signs of radiculopathy, obvious fracture, nerve damage, or acute cause of the low back pain. In addition, the review of past records does demonstrate that Patient D is approximately 10 cm shorter in height than five years ago. She clearly needs a work-up for osteoporosis.

The key to diagnosis is a thorough history and physical examination, followed by bone measurement tests. Because low BMD may indicate metabolic bone disease other than osteoporosis (e.g., hyperparathyroidism or osteomalacia), it should not be used as the sole indicator of osteoporosis [20]. Healthcare professionals should also ask about other risk factors for osteoporosis, as well as any family history, pain or tenderness in bones or joints, recent broken bones, current and recent past medication use, and level of physical activity. For men, physicians should inquire about changes in libido. On exam, it is important that height is measured and compared with results from past measurements. There also should be a focus on evidence of old fractures during a skeletal survey, as previous fractures often may signal the presence of osteoporosis or a metabolic abnormality. If suspicion for osteoporosis is high, bone measurement testing should follow.

Patient D has a full chemistry panel including calcium and phosphorus, liver function tests, thyroid function tests, and a complete blood count (CBC). All are within normal limits. Normal values should not be unexpected in patients with osteoporosis, as this is often the case. Because suspicion remains high for osteoporosis, Patient D must undergo bone mineral density testing. Although the patient wishes to have an x-ray, simple x-rays would not be helpful here unless one is trying to rule out a fracture or other structural cause of the low back pain.

BONE DENSITY MEASUREMENT TESTS

There are several ways to determine bone mineral density, and each diagnostic tool may identify a different population with osteoporosis. Bone measurement tests include DXA of the hip, spine, or wrist; quantitative ultrasound of the heel; spinal CT; radiographic absorptiometry; and MRI. These tests are most useful when they will have an effect on clinical decision making. That is, physicians should have a plan before they order a test and anticipate how the test result will affect their management of the patient.

There is considerable debate among the several disciplines that perform bone density studies. Osteoporosis clinics using DXA have their preferences, while radiologists performing CT scans or MRI may have different ideas. The spectrum of available tests is outlined here, but most authorities now prefer DXA [20; 31; 34; 35; 36]. The types of studies performed and their appropriate follow-up times continue to be investigated at many centers. For additional information, one may review the Official Positions of the ISCD [33].

Dual-Energy X-Ray Absorptiometry

The most commonly used BMD assessment is DXA, which may be done either at central or peripheral (pDXA) sites. DXA uses two distinct beams of x-ray photons. The amounts of each x-ray beam that pass through bone and soft tissue are compared to estimate the bone density. DXA measures the sum of cortical and trabecular bone and can detect as little as 2% bone loss. Central DXA measures BMD at the spine, upper femur, and hip, whereas pDXA

measures BMD at the heel, finger, and forearm. Measurement of hip BMD represents a good approach because there is less soft tissue and other artifacts compared to other sites. Individuals with osteoporosis have a greater risk of fractures in the hip and spine, which can lead to longer recovery time, greater pain, and permanent disability [23; 37]. These sites also are appropriate for monitoring the effectiveness of therapy, as they are more likely to show an increase in BMD in response to treatment [23]. Be aware, however, that falsely elevated BMD may occur in patients with certain pathologic processes, such as degenerative joint disease, compression fractures, and vascular calcifications.

Central DXA is generally preferred over pDXA as it can measure whole body bone mass. It has minimal radiation exposure and may be completed in less than 10 to 15 minutes [37]. Peripheral DXA may be done with portable units in a physician's office and involves even less radiation than central DXA. It is also less expensive. However, it is less sensitive and less specific and thereby provides less precise T-scores. Moreover, pDXA cannot detect spinal fracture sites. It is most useful at identifying at-risk individuals who may benefit from further BMD testing [23; 37].

Quantitative Ultrasound

Quantitative ultrasound is based on the premise that attenuation of sound waves into bone and the speed of sound correlate independently with BMD of the heel. The calcaneus is the primary site of measurement, although this technique also has been used to measure bone mass at the tibia, phalanges, or wrist. It is believed that ultrasound measures changes in bone architecture. Limitations include measure reproducibility (should not be used for monitoring bone changes over time or to evaluate response to therapy) as well as lack of adaptation for various sizes and shapes of heels. It involves no radiation exposure, but it is less sensitive than DXA and does not always correlate with DXA readings. However, some studies have indicated that quantitative ultrasound may predict fractures as well as other measures of bone density [20; 21; 38].

Quantitative Computed Tomography

Quantitative CT can measure the lumbar spine, hip, and peripheral sites. In general, the results are less likely to be affected by degenerative spinal changes than spinal DXA scanning. Unlike DXA, quantitative CT allows for assessment of both cortical and trabecular bone. As a result, it can make volume BMD determinations [20]. Trabecular bone, because of its higher rate of turnover compared with cortical bone, is expected to show metabolic changes earlier [39]. The ability of quantitative CT to enable prediction of spinal fracture is equal to that of DXA scanning in postmenopausal women; there is lack of sufficient evidence for fracture prediction in men [20]. The cost and level of radiation exposure are higher (as much as 200 times greater than some other techniques) [20]. In some cases, this results in decreased patient acceptability.

Radiographic Absorptiometry

Radiographic absorptiometry provides radiologic assessment of the metacarpals and phalanges. It was originally based on a plain film; however, computerized image processing has since been applied to radiography [40]. Radiographs are an insensitive measure of bone loss and may only demonstrate abnormalities after 30% of bone loss has occurred [41]. Generally, radiographic absorptiometry is not recommended as a screening or diagnostic test for osteoporosis or osteopenia. It can be used to assess vertebral and overall fracture risk in postmenopausal women; there is lack of sufficient evidence for fracture prediction in men [20].

Magnetic Resonance Imaging

Most people today are familiar with MRI and aware that it uses a strong magnetic field, limiting its use in patients with ferromagnetic implants. Essentially, cells in the bony region studied emit a signal as they respond to the radio frequency waves of the device. The detector transmits the skeletal information to the computer, which then produces the familiar detailed images. MRI is valuable in the assessment of vertebral body fractures, nonspinal insufficiency fractures, bone mass and strength, and bone marrow edema. The signal-intensity characteristics of bone

BIOCHEMICAL MARKERS OF BONE FORMATION AND RESORPTION	
Formation Markers	**Resorption Markers**
Bone specific alkaline phosphatase (BSAP) Osteocalcin C-Amino-terminal propeptide of type I procollagen (PINP) Carboxy-terminal propeptide of type I collagen (PICP)	Calcium Hydroxyproline Free and total deoxypyridinolines (Dpd) Free and total pyridinolines (Pyd) Type I collagen cross-linked C-telopeptide (CTx) Type I collagen cross-linked N-telopeptide (NTX)
Source: [43; 44]	*Table 3*

marrow may allow the differentiation of neoplastic fractures from accompanying osteoporosis [41]. The use of MRI in diagnosing osteoporosis is still evolving and is unlikely to become widely used due to the expense and time required to obtain a scan [41]. Also, more research must be done to improve the sensitivity and specificity of MRI as well as to calculate appropriate T- and Z-scores. Its use, therefore, is mainly limited to certain centers, which generally use MRI for osteoporosis detection as part of a research study.

Selection of Tests

Given the multitude of tests, there are some general factors to keep in mind when ordering them. For women 65 years of age and younger, vertebral fractures are more common than hip fractures [42]. Therefore, it is prudent to also consider ordering DXA of the spine. For women older than 65 years of age, hip fractures are more common. At the same time, degenerative spinal changes and aortic calcifications make spine imaging more difficult to assess. Therefore, one should consider DXA of the hip or lateral spine, as well as quantitative CT of the hip. DXA of the hip is the best predictor of future hip fracture risk [20]. DXA is also preferred when patients exhibit multiple risk factors. Measurements at two sites are preferable, as this increases sensitivity and specificity. Again, these are general considerations; individual physician's preferences may differ.

Serial measurements may be helpful to assess bone loss rates; however, they should not be performed too often. Follow-up measurements, one to two years apart, may be useful in determining whether patients with normal baseline bone mass demonstrate a rapid loss of BMD. They may also be helpful when assessing persons undergoing treatment to discern whether the treatment has been effective [20]. Presently, DXA is the only method that has been validated for use in serial measurements. Keep in mind that a minimum of two years is typically required to measure any changes in BMD [6; 20].

Patient D should undergo DXA of the hip. She has a history of degenerative joint disease, which makes spine-imaging results more difficult to interpret. In addition, she has numerous risk factors, which make DXA a preferred test.

LABORATORY TESTS AND BIOCHEMICAL MARKERS

There are currently no specific laboratory tests of blood or urine that are diagnostic of osteoporosis. Most laboratory tests will be normal. A physician or other clinical provider, however, should still order lab tests that include a complete serum chemistry, including calcium and phosphorus, CBC, thyroid function tests, parathyroid hormone (PTH), 25-hydroxyvitamin D, free testosterone, liver function tests, and urine calcium, in order to diagnose secondary causes, such as hyperthyroidism or hyperparathyroidism [6].

The strength of bone is determined by bone density and bone quality, but the overall rate of remodeling also plays an important role. The remodeling process, including the breakdown of bone and protein matrix, generates breakdown products, many of which may be measured in the blood or urine. Additionally, the formation of bone increases other markers (***Table 3***).

Studies of these biochemical markers have not been encouraging for their use in clinical practice, and their routine use in clinical practice is not generally recommended [35; 44]. The levels of the markers change daily, even hourly, so many measurements would have to be made to determine an accurate level. Although biochemical markers have not yet proven to be predictive of bone mineral density or fracture risk, studies have shown that they may be able to estimate fracture risk and rate of bone loss, particularly when combined with BMD [23; 31]. They have also demonstrated an early estimation of treatment effect [31].

RISK ASSESSMENT TOOLS

Assessment tools that may be used to determine a patient's osteoporosis risk include the Osteoporosis Risk Assessment Instrument (ORAI), the Simple Calculated Osteoporosis Risk Estimation (SCORE), and the WHO Fracture Risk Assessment Tool (FRAX).

The ORAI is a simple, three-item tool based on age, weight, and current hormone use. The SCORE tool combines six risk factors, including age, weight, race, estrogen use, presence of rheumatoid arthritis, and fracture history. A Canadian study using DXA of the hip as the standard for diagnosing osteoporosis (T-score below -2.5) found that the ORAI had a sensitivity of 97.5% and a specificity of 28%. In the same study, the SCORE tool had a higher sensitivity, at 99.6%, but a lower specificity, at 18% [45]. A systematic review of SCORE, ORAI, and the Osteoporosis Self-assessment Tool (OST) found SCORE and OST to have a higher sensitivity for predicting major osteoporotic fracture in women 65 years of age and older [46]. The OST uses age and weight as parameters to predict the risk of osteoporosis and has been found to be superior in identifying men at risk of osteoporosis or osteoporotic fractures [47; 48].

FRAX is a web-based tool that assesses the 10-year risk of a major osteoporosis fracture in women and men. Individual risk factors (i.e., age, sex, weight, height, and femoral neck BMD, if available) and clinical risk factors (i.e., prior fragility fracture, parental history of hip fracture, current tobacco use, long-term glucocorticoid use, rheumatoid arthritis, daily alcohol consumption, and secondary causes of osteoporosis) are entered into the web tool, which calculates and provides a 10-year fracture probability (as a percentage) of absolute, rather than relative, risk (as occurs on the output of DXA equipment) [43]. The BHOF has outlined U.S.-specific considerations for the application and use of FRAX [20]. The 2020 American Association of Clinical Endocrinologists and American College of Endocrinology (AACE/ACE) clinical practice guidelines for the diagnosis and treatment of postmenopausal osteoporosis recommend use of the FRAX algorithm as part of the initial evaluation and for guiding treatment decisions [49].

SCREENING GUIDELINES

Routine BMD screening has been recommended for women 65 years of age and older, regardless of risk, and for women 50 to 69 years of age with clinical risk factors for fracture (e.g., low body weight, prior fracture, high risk medication use, disease or condition associated with bone loss) [20; 33; 35; 50; 51]. The ISCD and BHOF also have recommended routine screening for men 70 years of age and older, regardless of risk factors, and for men 50 to 69 years of age when concerns exist about the patient's risk factor profile (e.g., low body weight, prior fracture, high risk medication use, disease or condition associated with bone loss) [20; 33]. The U.S. Preventive Services Task Force (USPSTF) has determined that the evidence is insufficient to recommend for or against routine screening for osteoporosis in men [50]. Additional recommendations for BMD screening include [20; 33; 35; 50; 51]:

- Adults being considered for pharmacologic therapy for osteoporosis
- Women in menopausal transition with risk factors for fracture
- Adults 50 years of age and older with fragility fracture
- Adults with disease/conditions associated with low bone mass/bone loss
- Anyone not receiving therapy in whom evidence of bone loss would lead to treatment

EVIDENCE-BASED PRACTICE RECOMMENDATION

The USPSTF recommends screening for osteoporosis with bone measurement testing to prevent osteoporotic fractures in women 65 years and older and postmenopausal women younger than 65 years who are at increased risk of osteoporosis, as determined by a formal clinical risk assessment tool.

(https://jamanetwork.com/journals/jama/fullarticle/2685995. Last accessed October 15, 2024.)

Strength of Recommendation: B (There is high certainty that the net benefit is moderate or there is moderate certainty that the net benefit is moderate to substantial.)

TREATMENT

The challenge for physicians and other clinicians is to diagnose, prevent, and treat osteoporosis before fractures occur. However, several studies have indicated that there has been a failure in the United States to apply preventive and treatment measures to many individuals at risk for bone disease [23]. For example, the use of BMD testing in this at-risk population has been estimated to be as low as 3%; calcium and vitamin D supplementation has been recommended to only 11% to 14% of this population; and antiresorptive therapy has been recommended for only 12% to 16% of this population [52; 53]. Additionally, Medicare cuts in reimbursement for DXA services (initiated in 2007) led to a decline in office-based provision of DXA services, a decline in retail prescriptions for osteoporosis therapies, and a decline in restarting drug therapy after an extended gap in treatment, despite a 2.6% increase in the U.S. population aged 65 years and older [54; 55; 56]. One retrospective analysis found a significant association between Medicare reimbursement reductions and decreased use of BMD testing in female Medicare beneficiaries who had no supplemental private health insurance [57].

According to BHOF guidelines, postmenopausal women and men 50 years of age and older who present with any of the following should be considered for treatment [20]:

- Hip or vertebral (clinical or morphometric) fracture
- T-score at the femoral neck or spine of <-2.5 (after evaluation has excluded secondary causes)
- Low bone mass (T-score between -1.0 and -2.5 at femoral neck or spine) and 10-year probability of hip fracture >3% or 10-year probability of major osteoporosis-related fracture >20%

These recommendations also are supported by the AACE/ACE [49]. Although the guidelines are helpful, it is important to remember that treatment should be considered on an individual basis because T- and Z-scores are only part of a patient's workup [20; 58].

Numerous treatment options exist, including [20]:

- Diet/supplementation
- Exercise
- Medications

Some patients may have a limited English proficiency, requiring the need of translators or foreign language brochures to properly convey the necessary information.

DIET/SUPPLEMENTATION

Calcium

The skeletal structures contain 99% of the body's calcium stores. When the extraskeletal calcium level is inadequate, bone tissues are resorbed in an attempt to maintain equilibrium. To prevent excessive skeletal calcium loss, an adequate amount of calcium, as well as vitamin D, must be ingested. Clinical trials have shown that following a regimen of adequate consumption of calcium and vitamin D may significantly reduce fracture risk [20].

According to BHOF recommendations, men 50 to 70 years of age should obtain at least 1,000 mg/day of elemental calcium; women 51 years of age and older and men 71 years of age and older require 1,200 mg/day of elemental calcium [20]. National nutrition surveys have revealed that many individuals in the United States consume less than half of

the recommended daily amount of calcium in their diet [20]. Dietary supplements may be necessary. Intakes in excess of 1,200–1,500 mg per day provide limited benefit and may increase the risk of developing kidney stones or cardiovascular disease [20]. The upper safe limit for total calcium intake is 2,500 mg/day [23; 59].

Calcium supplements are especially necessary in more fragile, older osteoporosis patients; however, the problem of reduced calcium absorption is more acute in older persons. This may be overcome by increasing overall calcium intake and maintaining adequate levels of vitamin D [23]. The best way to increase calcium intake is through diet (e.g., consumption of dairy products), because supplements are not always absorbed well. To increase absorption, supplements should be taken with meals [23]. For patients on acid-reducing medications, calcium citrate should be used because calcium carbonate requires an acidic environment.

Vitamin D

Normally, vitamin D is mainly stimulated by ultraviolet radiation, or sunlight, on the skin and then by hydroxylation in the liver and kidney. Vitamin D then acts to increase intestinal absorption of calcium and promote bone formation. Deficiency of vitamin D in children causes rickets, and adult deficiency results in osteomalacia. Because it is not practical for many individuals to get adequate levels of vitamin D from exposure to sunlight, increasing vitamin D levels through diet and supplementation should be encouraged [23]. Vitamin D supplementation in conjunction with calcium has been shown to reduce fractures [21].

According to BHOF recommendations, adults 50 years of age and older should obtain 800–1,000 IU of vitamin D per day; AACE/ACE guidelines recommend 1,000–2,000 IU to maintain optimal serum 25 hydroxyvitamin D levels [20; 49]. High-risk patients (e.g., the elderly) may need more. The safe upper limit of daily vitamin D intake for the general adult population was increased to 4,000 IU/day in 2010 [60]. Evidence has shown that higher daily intakes are safe and that some elderly patients may need this amount to maintain optimal serum 25 hydroxyvitamin D levels [20; 49]. Keep in mind that both vitamin D and calcium supplements should be combined with other treatments.

Phytoestrogens

Plant-derived phytoestrogens may be found in such foods as beans, cabbage, rice, berries, sesame seeds, and grains. They are structurally similar to estrogen, but with weaker effects. They also are not stored in the body and may be easily broken down and eliminated. The three main dietary types of phytoestrogens are isoflavones, coumestans, and lignans. Most foods that contain these compounds include more than one type [61].

Most evidence about the potential role of phytoestrogens has been based on animal studies, and many of these studies have shown that treatment with phytoestrogens has serious adverse effects [62; 63; 64]. Phytoestrogens also have been associated with some serious drawbacks, including inability to accurately measure their levels in food; limited scientific evidence regarding active ingredients, dosage, and potential presence of unexpected agents; and a short-lived benefit cycle [65; 66]. Additionally, the evidence in humans remains conflicting [61; 67]. Few studies on the effect of phytoestrogens on BMD have shown a positive effect; supplementation is not recommended [68; 69; 70; 71].

EXERCISE

Exercise is beneficial for many reasons, including reduction in the risk of heart disease, improved glycemic control in diabetes, improved blood pressure, and reduction in cholesterol levels (total cholesterol and low-density lipoprotein [LDL]), as well as improved psychologic well-being. For patients with osteoporosis, exercise may specifically increase bone mass and total body calcium. Numerous studies have documented that consistently active individuals have higher bone density than inactive individuals [23]. The beneficial physiologic effects most likely result from imposing repetitive stress upon the muscular and skeletal systems. The mechanical strain and loading on bone may decrease the rate of bone loss as well as produce an actual increase in bone mass [23].

Exercises can basically be classified as either aerobic or anaerobic. Aerobic exercise is any activity that uses large muscle groups, is maintained continuously, and is rhythmic in nature. It strengthens the myocardium and improves overall fitness by increasing the body's ability to use oxygen. It does so by increasing the inotropic and chronotropic activity of the heart along with increasing respiratory demand. Examples of aerobic exercise include running, biking, skating, brisk walking, and dancing. Anaerobic exercises typically involve major muscle groups and resistance training, which relate to muscular strength and muscular endurance. Muscular strength involves exerting a force for a brief period of time with repeat contractions until the muscle becomes fatigued. Weightlifting is a good example of an anaerobic muscular strength activity. Muscular endurance involves sustaining repeated contractions or the application of a continual force against a fixed object. Push-ups are an example of muscular endurance. The BHOF has recommended a combination of weight-bearing and resistance type (i.e., muscle strengthening) exercises [20]. The program prescribed will depend on the ability and interests of the individual patient. Patients should be encouraged to exercise at least 30 minutes per day, at least five days per week, eventually working up to 60 minutes per day, if tolerated. Ideally, patients should stretch for 10 minutes prior to exercise. Patients with a history of vertebral compression fracture, as well as those patients with significant musculoskeletal disease or serious degenerative joint disease, should initially participate in a monitored exercise program [11].

MEDICATION

Medications may be divided into antiresorptives, which reduce bone loss, and anabolic, or bone-formation, agents. Antiresorptive therapies include estrogen, selective estrogen receptor modulators (SERMs), bisphosphonates, and calcitonin. The first U.S. Food and Drug Administration (FDA)-approved anabolic agent was teriparatide, which is a synthetic form of PTH. A second agent, abaloparatide, was approved by the FDA in 2017 for the treatment of osteoporosis in postmenopausal women at high risk for fracture [72; 73]. A third anabolic agent, romosozumab, was approved by the FDA in 2019 [74]. The effectiveness of these therapies, and combinations of them, is being studied [23].

Antiresorptives

Hormone Replacement

Hormone replacement, either in the form of unopposed estrogen or estrogen-progestin combination agents, had commonly been used in postmenopausal patients for alleviation of postmenopausal symptoms and prevention of chronic diseases. Estrogen increases osteoblastic activity, which leads to greater pro-collagen and alkaline phosphatase production. As a result, it inhibits bone resorption. Deficiency in estrogen causes increased osteoclast formation. Studies conducted in the early 2000s have led to a change in the recommendations for hormone therapy in postmenopausal women [20; 36; 75].

The WHI, a large randomized control trial (and an observational study), showed the osteoporosis prevention benefit of combination therapy in healthy, postmenopausal women. Nearly 27,000 women were randomized to conjugated estrogen plus medroxyprogesterone (if they had an intact uterus), conjugated estrogen (if they had a hysterectomy), or placebo. The primary outcome measure was coronary heart disease, but hip fracture was one of the secondary outcomes measured. The results demonstrated a one-third decrease in hip fractures and a 24% to 30% decrease in total fractures among the treatment group [13; 23]. The reduction in total fracture risk was significant; however, reductions in vertebral and hip fractures were not statistically significant. The study was stopped before completion due to increases in invasive breast cancer in the treatment group. There was also an increased absolute risk of nonfatal stroke, cognitive impairment, venous thromboembolism, and nonfatal myocardial infarction. A reduced incidence in colon cancer was

observed. The authors concluded that hormone replacement is not recommended unless the fracture risk benefit is greater than the risk of cardiovascular disease and breast cancer [13; 23].

Another trial, the Heart and Estrogen/Progestin Replacement Study (HERS) and its subsequent follow-up HERS II, studied more than 2,700 postmenopausal women with pre-existing coronary heart disease and an intact uterus. Patients were randomized to conjugated estrogen plus medroxyprogesterone daily versus placebo. The studies involved a mean follow-up of 4.1 years. No significant decrease in hip or total fracture rates was shown for the patients receiving daily combination therapy [76]. The HERS trial showed no protective cardiovascular effects of the treatment and actually showed a 50% increase in cardiovascular events in the treatment group in the first year of the trial. The HERS II trial supported the conclusion from the initial HERS study, which was that hormone replacement therapy does not reduce the risk of cardiovascular events in postmenopausal women with coronary heart disease.

Prior to the studies, hormone replacement therapy was generally considered beneficial; however, recommendations have changed. The USPSTF has recommended against routine use of combination hormone therapy for prevention of chronic disease in postmenopausal women. The USPSTF also has recommended against routine use of unopposed estrogen in patients who have undergone a hysterectomy [77]. Hormone replacement therapy has been implicated in increased risk of breast cancer, stroke, venous thromboembolism, cholecystitis, and possibly coronary heart disease. Unopposed estrogen also has been shown to increase the risk of endometrial cancer. The WHI, HERS, and HERS II studies helped form an argument against hormone therapy in postmenopausal women, and given the other effective treatments for osteoporosis, treatment with hormones is not recommended [77].

While the WHI study findings have been useful, it should be noted that concerns have arisen in response to their conclusions. Specifically, the high average age of the study population (63.3 years of age) and use of only one type of medication and dosage have been the source of much criticism. It is necessary to remember that the use of hormone therapy should be individualized to the patient's needs and medical history. Hormone replacement therapy may be beneficial short-term for a small subset of women with severe fracture risk [23].

The AACE has suggested that hormone replacement could be acceptable for treatment of osteoporosis under the following circumstances, after obtaining informed consent, discussing the risks and benefits of replacement, and with strict follow-up [36]:

- Women with significant menopausal symptoms who are at risk for osteoporosis
- Women with significant osteoporosis who are unable to tolerate alternative therapies

When used to treat menopausal symptoms, estrogen should be used at the lowest necessary dosage and for the shortest possible time [49]. Because research is ongoing in this area, recommendations may evolve or change.

Selective Estrogen Receptor Modulators

SERMs are designed to mimic the beneficial effects of estrogen on bone, the heart, and the central nervous system, while at the same time minimizing the adverse effects on the breast and the uterus [23]. For example, raloxifene is an estrogen receptor modulator that acts as an estrogen agonist for bone and the lipoproteins, but an antagonist at the breast and uterus. It was the first SERM approved for the prevention and treatment of osteoporosis in postmenopausal women and has been shown to increase BMD, structurally recover bone, and decrease the risk of vertebral fractures [78; 79]. It is contraindicated in patients with a history of clotting disorders, such as venous thromboembolism. Side effects include leg cramps, arthralgias, rhinitis, headaches, and hot flashes [73; 79].

The Multiple Outcomes of Raloxifene Evaluation (MORE) trial was a multicenter, randomized, double-blind, placebo-controlled study that followed 7,705 postmenopausal women for three years. The MORE trial demonstrated a decreased risk of invasive breast cancer by 76% as well as increased bone density in the spine and femoral neck and significantly reduced risk of vertebral (but not hip) fractures [80; 81].

Interestingly, some data have suggested that raloxifene may reduce coronary events and strokes in women at high risk for cardiovascular events and lower cholesterol levels, similar to statins [79]. Additional research is being conducted with respect to these outcomes [82].

Tibolone is an estrogen-like agent that has been used for decades in Europe to reduce menopausal symptoms and possibly prevent bone loss. Although there is some evidence of an increased risk of stroke, it does not appear to stimulate breast or uterine tissue and has been suggested for use in the treatment of vasomotor symptoms and prevention of osteoporosis [83]. However, it is not currently approved by the FDA for use in the United States [73].

Another SERM, bazedoxifene, was approved for the treatment of osteoporosis by the European Medicines Agency in 2009 [84]. One randomized, controlled trial of postmenopausal women with osteoporosis compared 20 mg or 40 mg of bazedoxifene with 60 mg raloxifene or placebo [85]. After 36 months, the incidence of new vertebral fractures was significantly lower in all treatment groups compared to placebo. Bazedoxifene also improved BMD and reduced bone marker levels. FDA approval of bazedoxifene was granted in 2013 [73; 86].

Bisphosphonates

Bisphosphonates act to decrease resorption by causing apoptosis and decreased function of osteoclasts. Several medications or drug combinations have been approved by the FDA for the prevention and treatment of osteoporosis, including alendronate, alendronate plus D (alendronate and cholecalciferol), ibandronate, risedronate, risedronate with a calcium supplement, and zoledronic acid [20]. These agents may also be effective in reversing the effects of steroid-induced osteoporosis [73; 87]. The FDA also has approved the use of other bisphosphonates, including etidronate disodium, pamidronate, and tiludronate; however, they have not been approved for use in osteoporosis [73; 88].

According to the Institute for Clinical Systems Improvement, bisphosphonates should be considered (unless contraindicated) for reduction of fracture risk (both vertebral and non-vertebral) in men and postmenopausal women with osteoporosis.

(https://www.icsi.org/wp-content/uploads/2019/01/Osteo.pdf. Last accessed October 15, 2024.)

Strength of Recommendation/Level of Evidence: Strong recommendation, high-quality evidence

For severe osteoporosis, bisphosphonates are the best treatment option, with beneficial effects typically seen within a year. Note that bisphosphonates should be used with caution in patients with severe renal impairment [20; 73].

Oral bisphosphonates are generally well-tolerated; however, complaints of upper gastrointestinal side effects (e.g., dyspepsia, reflux) are common in adults [20; 73]. When side effects occur and threaten to interfere with therapy, evaluate the patient's ability to comply with dosing instructions (e.g., take on empty stomach with 8 ounces water, remain upright 30 to 60 minutes) [20; 73]. If esophagitis/gastritis associated with alendronate is suspected, discontinue therapy for four to six weeks. Some patients may benefit from a change to risedronate; however, studies have found similar gastrointestinal tolerability between risedronate and alendronate [89; 90]. Intravenous bisphosphonates may be used in patients who are unable to tolerate oral preparations. IV zoledronic acid (preferred) is administered once every year (for treatment) or once every two years (for prevention); ibandronate is administered once every three months [73; 91].

Results after three years of therapy with oral bisphosphonates vary across studies. Generally, femoral neck and spine BMD have increased by 1.5% to 6% and 5.5% to 6.5%, respectively, and vertebral/femoral neck fracture risk has been reduced by 40% to 60%, a significant difference from trial placebo groups [92]. A 2017 meta-analysis of 24 studies was conducted to evaluate the efficacy of bisphosphonates in preventing fracture in patients with osteoporosis. The analysis included 21,335 patients assigned to a bisphosphonate group and 17,862 patients assigned to a placebo group [93]. The overall rate of osteoporotic fracture was 5.9% in the bisphosphonate group and 9.9% in the placebo group. The rate of vertebral fracture was 5.9% in the bisphosphonate and 10.3% in the placebo group. The rate of nonvertebral fracture was 6.9% in the bisphosphonate group and 9.6% in the placebo group [93]. The best long-term (5 to 10 years) data come from the use of alendronate [94; 95; 96].

There is no consensus on the optimal duration of bisphosphonate treatment [97; 98]. Generally, it is considered reasonable to discontinue treatment ("drug holiday"), after five years of oral therapy or three years of IV therapy, in low-risk women with stable BMD and no previous history of vertebral/femoral fracture [49; 99]. Most experts favor continuing therapy for high-risk patients (i.e., previous fracture, elderly/frail). The duration of drug holiday is a matter for clinical judgment and individual patient considerations, determined in part by annual BMD monitoring and the patient's level of activity and fracture risk [49; 100].

Alendronate, a second-generation bisphosphonate, has been shown to be most effective for patients with T-scores less than -2.5 or for patients with previous vertebral fracture. Alendronate has demonstrated the ability to reduce the incidence of wrist, hip, and spinal fractures by 50% over a three-year period in women with a prior fracture of the spine [20]. In the Fracture Intervention Trial (FIT), a large alendronate study, women with osteoporosis and vertebral fracture showed a significant decrease in vertebral and hip fractures [101]. A follow-up trial to FIT, the Fracture Intervention Trial Long-Term Extension (FLEX), showed that when compared with women who stopped alendronate after an average of five years, women who continued alendronate maintained a higher BMD and greater reduction of bone turnover. The risk for vertebral fracture between the two groups was relatively the same. While results indicated that women with very high risk of clinical vertebral fractures may benefit by continuing alendronate beyond five years, study results indicated that more data are needed on the effect of continuation versus discontinuation of alendronate before an optimal length of treatment can be recommended [94; 97]. One study sought to predict fracture risk among participants in the FLEX trial by looking only at those assigned to the placebo group [96]. Hip and spine DXA and two biochemical markers of bone turnover were measured when placebo was begun (FLEX baseline) and again after one and three years of follow-up. During five years of placebo, 22% of women in the placebo group experienced one or more symptomatic fractures and 19% had fractures after one year. Age and hip BMD at discontinuation predicted clinical fractures during the subsequent five years [96]. In both the FIT and follow-up FLEX trials, women were encouraged to take 500 mg/day of calcium and 250 IU/day of vitamin D in addition to the alendronate. One study suggests that the success of alendronate therapy may depend on the vitamin D status of patients [102].

Alendronate dosing is 5 mg/day for osteoporosis prevention and 10 mg/day for treatment [73; 103]. It is also available in a 35-mg and a 70-mg once-weekly oral dose that may be better for patient compliance due to its easier dosing. As stated, bisphosphonate medications should be taken on an empty stomach with a full glass of water. The most common side effects of alendronate are gastrointestinal, including esophagitis and gastric ulcer. Muscular and skeletal pains have also been reported. As stated, to prevent the gastrointestinal effects, the patient is urged to sit upright for at least 30 minutes after taking the medication [73]. Proton pump inhibitors and other acid reducing agents do not appear to prevent the gastrointestinal side effects of the bisphosphonates [103].

Of note, the effects of alendronate on bone density after discontinuation of hormone replacement therapy have yielded promising, if mixed, results. For example, in a published randomized controlled trial, women who had been diagnosed as having low BMD and had recently stopped hormone replacement therapy were randomized to either 10 mg of alendronate or placebo. At the end of the one-year trial, treatment with alendronate had demonstrated a 2.3% mean increase in spine BMD versus a mean loss of 3.2% in the placebo group. There was also greater total body and hip BMD preservation as well as decreased bone turnover with the use of alendronate as compared to placebo [104]. A separate trial, designed to evaluate the combined use of alendronate and estrogen, indicated that combination therapy produced somewhat larger increases in BMD than either agent alone and was well tolerated [105]. A trial designed to determine the rate of bone loss when therapy with alendronate, estrogen, or both agents was discontinued revealed accelerated bone loss after withdrawal of estrogen therapy, but not after withdrawal of alendronate or combination therapy [106]. One randomized, placebo-controlled trial compared BMD and bone turnover changes after therapy withdrawal in postmenopausal women treated with alendronate or estrogen/progestin [107]. Of the 1,609 women at the start of the trial, one-third were switched from alendronate to placebo after the second year and one-third after the fourth year (while all remained blinded to treatment assignment). Women taking estrogen/progestin in years 1 to 4 were followed off therapy in years 5 and 6. BMD decreased steadily in the placebo group during all six years, whereas spine and hip BMD increased during the first four years in groups receiving both alendronate and estrogen/progestin. BMD decreased during years 5 and 6 in the group previously treated with alendronate for four years. In comparison, large BMD decreases were observed at the spine and hip among women who received estrogen/progestin for four years [107].

Risedronate is another agent that is effective for osteoporosis. A three-year trial of risedronate on patients with pre-existing vertebral fracture demonstrated a significant reduction in both vertebral and nonvertebral fractures [108]. It reduced the incidence of fractures of the spine by 41% to 49% and other fractures by 36% in patients with prior spinal fractures [20].

The recommended dose of risedronate is 5 mg/day, or a 35 mg weekly dose for both treatment and prevention [20; 73]. The 35 mg dose of risedronate should be taken weekly with 1250 mg of calcium carbonate taken daily on the intervening six days. Reported side effects include headache, nausea, arthralgias, asthenia, abdominal pain, and other gastrointestinal problems [73]. A two-year study of risedronate given at a dose of 150 mg once a month to women with postmenopausal osteoporosis found similar efficacy and safety compared with risedronate 5 mg daily [109]. The mean percent changes in BMD at the hip and in biochemical markers of bone turnover were similar, as were adverse events.

Ibandronate also has been added to the FDA-approved list for the prevention and treatment of postmenopausal osteoporosis. The medication has been shown to reduce the incidence of spinal fractures by approximately 50% over a three-year period. It may be taken in tablet form, 150-mg tablet once a month, or intravenously, 3 mg every three months [73]. The side effects are similar to those of the other bisphosphonate medications [20; 73].

Denosumab

Denosumab is a human monoclonal antibody being studied for its effects on bone metastases, rheumatoid arthritis, and multiple myeloma [110; 111]. In 2011, the FDA approved denosumab for treatment of osteoporosis in postmenopausal women who are at high risk of fracture [73; 112; 113]. Denosumab acts by binding to and inhibiting receptor activator of nuclear factor kappaB ligand (RANKL). RANKL

controls the differentiation, proliferation, and survival of osteoclasts. Inhibition of RANKL provides a lengthened period of absorption, inhibition of bone resorption, and higher BMD [20; 73; 114]. Dosing of denosumab is 60 mg subcutaneous injection every six months.

Several studies evaluating the efficacy of denosumab in the prevention and treatment of postmenopausal osteoporosis have been completed. In the Fracture Reduction Evaluation of Denosumab in Osteoporosis every 6 Months (FREEDOM) trial, use of denosumab resulted in a reduced risk for vertebral, nonvertebral, and hip fractures in women with osteoporosis [115]. The trial involved 7,868 postmenopausal women with T-scores between -2.5 and -4 who were randomly assigned to receive placebo or a subcutaneous injection of 60 mg denosumab every 6 months for 36 months. Results demonstrated a 68% decrease in new vertebral fracture in the treatment group as compared to the placebo group (2.3% versus 7.2%) [115]. Significant reductions in hip and nonvertebral fractures were also noted. The authors reported no increases in adverse effects (e.g., cancer, delayed healing, osteonecrosis of the jaw, injection site reactions) associated with use of denosumab.

While results of one meta-analysis also found a decreased risk of nonvertebral fracture with use of denosumab in postmenopausal women with osteoporosis or low BMD, the study did find a significantly increased risk of serious adverse event related to infection [116]. A 12-month study compared the effects on BMD and bone turnover on patients with osteoporosis who were suboptimally adherent to bisphosphonates (and at higher risk for fracture) who were transitioned to denosumab or monthly oral bisphosphonate (ibandronate or risedronate) [117]. A total of 1,703 women were randomized to either denosumab 60 mg subcutaneously every six months or oral bisphosphonate 150 mg monthly. In both the overall and higher-risk populations, denosumab was associated with greater gains in BMD at 12 months than oral bisphosphonate at the total hip, femoral neck, and lumbar spine. Adverse events were generally similar between the two treatment groups [117]. Long-term use of denosumab is associated with a significant (48%) reduction in risk of all upper limb fractures and a 43%, 43%, and 58% reduction, respectively, in risk of forearm, wrist, and humerus fractures at seven years [118; 119].

Calcitonin

Calcitonin is a hormone normally produced by the parafollicular cells of the thyroid gland. Recombinant salmon calcitonin is approved by the FDA for the treatment and prevention of osteoporosis in women who have been postmenopausal for at least five years; it has not been recommended as a first-line treatment [20; 35]. In the proper dosages, it is an inhibitor of bone resorption [20; 23]. Calcitonin may be administered by intranasal spray or by a subcutaneous injection of 100 IU/day. Intranasal use has been shown to decrease vertebral fractures in patients with pre-existing fractures, but only at 200 IU/day, not at 100 IU or 400 IU/day [20; 21; 23]. Oral and inhaled forms of calcitonin are under development [23].

There is no good data regarding the use of calcitonin in reducing hip fractures or preventing any fractures in patients without pre-existing fracture [35; 49]. Calcitonin may have a role in patients with acute vertebral fractures due to a possible analgesic effect and its decreased risk of gastrointestinal upset and venous thromboembolism associated with other agents [120]. It has been shown to preserve bone mass by about 3% in the first year of glucocorticoid therapy [121].

Adverse effects from the injectable form include nausea, back pain, frequent urination, arthralgias, and rash. The intranasal form has fewer side effects, which are primarily localized and include rhinitis and, rarely, epistaxis [20; 73; 122].

Bone-Formation Agents

The original FDA-approved medications for osteoporosis were antiresorptives. Newer medications act instead to enhance bone formation by increasing the number and action of osteoblasts. The human PTH agents teriparatide and abaloparatide have been approved for use in the treatment of osteoporosis in patients with very high fracture risk [72; 73].

Parathyroid Hormone

PTH acts normally to increase bone resorption in response to low serum calcium levels; however, in intermittent doses, it has been shown to have a favorable impact on bone mineral density [23]. Teriparatide is a portion of human PTH, classified as PTH (1–34) and, as noted, has been approved by the FDA for the treatment of osteoporosis in postmenopausal women at high risk for a fracture. It also has been approved to increase bone mass in men with primary or hypogonadal osteoporosis who are at high risk for a fracture [20; 23; 36; 73; 123]. The FDA has approved an expanded indication for teriparatide for treatment of osteoporosis associated with sustained systemic glucocorticoid therapy (≥5 mg/day of prednisone). For this indication, teriparatide is available as 20 mcg once daily subcutaneous injection [20; 73]. Biosimilar preparations are now available, as the patent expired in 2019 [20].

Teriparatide stimulates new bone formation by increasing the number and action of osteoblasts. Specifically, it increases the number of osteoblasts through the induction of osteoprogenitor cell differentiation in the bone marrow. In addition, it prevents osteoblast apoptosis. It is offered as a daily injection and recommended for use in patients with severe osteoporosis, especially those who have failed other treatments [73]. In a pivotal trial of more than 1,500 postmenopausal women, there was a 65% reduction in new vertebral fractures compared with placebo over 19 months of treatment. New nonvertebral fractures were reduced by 56% [20]. Ninety-six percent of women had an increase in BMD. Side effects included nausea, leg cramps, and dizziness [124].

Treatment with teriparatide is not recommended for more than 18 months to 2 years, nor should it be prescribed to patients with pre-existing hypercalcemia [73; 123]. Before it may be prescribed, it is necessary to obtain baseline measurements of calcium, uric acid, current PTH level, creatinine, and 25 hydroxyvitamin D to be certain that hypercalcemia is not present. These values should be re-examined periodically [73; 123]. Of note, there was an increase in the incidence of osteosarcoma in rats that was dependent on dose and duration of treatment, although no cases of osteosarcoma were reported in patients during the clinical trials. Teriparatide should not be prescribed for patients at increased risk for osteosarcoma, patients with Paget disease or unexplained elevations of alkaline phosphatase, or those who have undergone prior skeletal radiation therapy [20; 73; 123].

Because prior use of the bisphosphonates may interfere with the action of PTH (1–34), it has been recommended that teriparatide only be administered to bisphosphonate-naïve patients [73; 123]. Side effects include leg cramps, dizziness, nausea, cramps, pharyngitis, asthenia, and headache [20; 73].

Like teriparatide, abaloparatide is a portion of human PTH, classified as PTH (1–34) and, as noted, has been approved by the FDA for the treatment of osteoporosis in postmenopausal women at high risk for a fracture [20; 72; 73]. Abaloparatide stimulates new bone formation by increasing the number and action of osteoblasts by acting as an agonist at the PTH1 receptor [73; 125; 126]. It is offered as a subcutaneous 80-mg daily injection [73]. As with teriparatide, abaloparatide therapy is not recommended for more than two years and is not recommended for patients with pre-existing hypercalcemia or an underlying hypercalcemic disorder (e.g., primary hyperparathyroidism) [73]. Before it is prescribed, it is necessary to obtain baseline measurements of calcium, uric acid, current PTH level, creatinine, and 25 hydroxyvitamin D to be certain that hypercalcemia is not present. These values should be re-examined periodically [73].

Abaloparatide has been shown to reduce the risk of new vertebral and nonvertebral fractures, major osteoporotic fractures, and clinical fractures, with a significant improvement in BMD at femoral neck, total hip, and lumbar spine [127; 128].

Romosozumab-aqqg

Romosozumab-aqqg is a monoclonal antibody that blocks the effects of the protein sclerostin and works mainly by increasing new bone formation [20; 74]. It is approved for the treatment of osteoporosis in postmenopausal women with a history of osteoporotic fracture, with multiple risk factors for fracture, or those who have failed or are intolerant to other osteoporosis therapies [20].

The result of two clinical trials involving more than 11,000 women with postmenopausal osteoporosis, one year of treatment with romosozumab-aqqg lowered the risk of vertebral fracture by 73% compared with placebo [74]. One dose consists of two injections, one immediately following the other, given once a month. The bone forming effect wanes after 12 doses, so more than 12 doses should not be used.

Romosozumab-aqqg has a boxed warning regarding an increase in the risk of heart attack, stroke, and cardiovascular death, and it should not be used in patients who have had a heart attack or stroke within the previous year. Other possible adverse effects include joint pain, headache, and injection site reactions [74].

Sodium Fluoride

Sodium fluoride is not currently a recommended treatment for osteoporosis based on the data available as well as significant side effects, including hyperostosis, gastrointestinal irritation, rash, and various neurologic complications. However, sodium fluoride does increase osteoblastic activity and has been shown to cause an increase in spine and hip bone mass [20; 123]. Initially, the new bone formed is poorly mineralized, but eventually it is replaced by the lamellar bone structure. Its effect on trabecular bone is more prominent than cortical bone. Significant effects on the rate of vertebral fracture have not been shown in any studies [21].

Vitamin D Analogues

Vitamin D causes increased gastrointestinal absorption of calcium, a function that is generally impaired in the elderly. Results from trials have shown decreased fracture rates in older patients taking vitamin D; it is often given in combination with calcium supplements in these patients [20]. The main concern with vitamin D supplementation is hypercalcemia, so calcium levels must be monitored. Vitamin D analogues also may cause gastrointestinal symptoms, erythema multiforme, and hyperphosphatemia. As noted, the common recommended daily dose of vitamin D is 800–1,000 IU, although there is not a clear consensus as to the optimal dose. Evidence indicates that higher intakes are safe and that some elderly patients will need at least 2,000 IU daily to maintain optimal serum levels [20; 49]. As previously stated, the safe upper limit for vitamin D intake was increased in 2010 to 4,000 IU daily for adults [60].

Calcitriol is a synthetic vitamin D analogue that has been approved by the FDA for managing hypocalcemia and metabolic bone disease in patients on renal dialysis, as well as for those with hypoparathyroidism [73]. There has not been a demonstrated reduction in osteoporotic fractures from the use of calcitriol [123].

Strontium ranelate is an investigational drug that inhibits bone resorption and stimulates bone formation [129; 130]. Large trials of strontium ranelate use in postmenopausal women with osteoporosis have shown a 40% to 50% reduction in the risk of vertebral fractures as well as a reduction in the risk of nonvertebral fractures; a separate review of the drug's efficacy concluded that it reduced vertebral fractures in postmenopausal women both with and without osteoporosis [131; 132; 133; 134; 135]. An open-label study examined the efficacy of strontium ranelate over 10 years in postmenopausal women with osteoporosis. Results indicate a continuous increase in BMD over the 10-year period and a lower incidence of both vertebral and nonvertebral fracture with use of strontium ranelate compared to placebo [136]. However, debate continues about whether the drug's effects on the vascular and neu-

rologic systems are sufficient to limit or abandon its use [137]. Other agents, such as insulin-like growth factors and bone morphogenic proteins, are also undergoing further research.

Some data have suggested that medications to treat osteoporosis have been underused and that too little of what has been learned about bone health has been applied in practice [23]. Reasons for such low treatment rates include lack of knowledge of the recommended therapies and inappropriate work-up following a fracture diagnosis.

Patient D's T-score from DXA of the hip is -2.5; she meets the WHO criteria for osteoporosis. Given that she is already experiencing symptoms, intervention is necessary. A review of diet is the first step. Patient D currently does not use any supplements because she believes she eats a healthy diet. However, further review with a dietitian reveals that she is below the recommended intake of calcium and vitamin D. Therefore, supplementation with both calcium and vitamin D should begin immediately. As noted earlier, Patient D tries to remain active, mostly involved in walking and gardening. These can be good aerobic exercises, depending on their intensity, and she should be encouraged to continue them. However, a weight-bearing exercise regimen should slowly be worked into her routine. Because she does have degenerative joint disease, a monitored exercise program should be initially pursued so that she focuses properly on form and does not cause any excess stress on her joints.

Medications should also be strongly considered, given her T-score as well as symptoms. SERMs and bisphosphonates should be the preferred medications. Estrogen replacement is not recommended.

TREATMENT MONITORING AND FOLLOW-UP

Because medications have side effects and proper diet/exercise may not be routinely followed, it is important to monitor treatment with BMD testing and to consider evaluating the level of the biochemical markers. There is no universally accepted agreement on treatment monitoring, including the utility of biochemical markers; however, some authorities have provided suggested guidelines for following patients being treated for osteoporosis [20; 36].

It has been noted that most treatment measures will produce minor increases in bone mass over the period of one year and that improvement may not be evident until after 24 months of treatment. In addition, most measurement errors are around 5%, so there will need to be improvement greater than 5% in bone mass to have any significance. Taking all of this into consideration, monitoring should occur every two years in most cases; however, the interval should be determined according to individual patient status [20; 33; 37].

DIAGNOSING AND TREATING OSTEOPOROSIS PATIENTS WITH THE ASSISTANCE OF AN INTERPRETER

As a result of the evolving racial and immigration demographics in the United States, interaction with patients for whom English is not a native language is inevitable. Because patient education is such a vital aspect of the treatment and management of osteoporosis, it is each practitioner's responsibility to ensure that information and instructions are explained in such a way that allows for patient understanding. When there is an obvious disconnect in the communication process between the practitioner and patient due to the patient's lack of proficiency in the English language, an interpreter is required. (In

many cases, the terms "interpreting" and "translating" are used interchangeably, but interpreting is specifically associated with oral communication while translating refers to written text.) While this may be easier said than done, due to institutional and/or patient barriers, the U.S. Department of Health and Human Services Office for Civil Rights has stated that denying adequate interpreter services to patients with limited English proficiency is a form of discrimination and that insufficient use of professional interpreters and inappropriate reliance on ad hoc interpreters may compromise patient care [138].

In this multicultural landscape, interpreters are a valuable resource to help bridge the communication and cultural gap between clients/patients and practitioners. Interpreters are more than passive agents who translate and transmit information back and forth from party to party. When they are enlisted and treated as part of the interdisciplinary clinical team, they serve as cultural brokers, who ultimately enhance the clinical encounter. In any case in which information regarding diagnostic procedures, treatment options, and medication/treatment measures are being provided, the use of an interpreter should be considered.

CONCLUSION

Osteoporosis is a significant health problem. Along with osteopenia, it affects a very large portion of the population. Unfortunately, it is often a silent disease, because patients typically do not present with signs and symptoms until they actually experience an untoward event, such as a fracture. Clinicians and patients should understand the factors that heighten the risk for developing osteoporosis, including advanced age, certain ethnicities, family history, and female gender. Particular attention should be directed to modifiable risk factors, such as tobacco use, physical inactivity, nutritional deficiencies, and medication usage.

The good news is that osteoporosis can be detected before significant symptoms occur. A complete history and physical examination, followed by BMD testing, such as DXA or other modality, can identify the majority of patients with osteoporosis. For patients who are diagnosed with osteoporosis or who are determined to be at risk, a plan of diet supplementation and frequent weight-bearing exercises may significantly improve bone structure. Numerous medications useful in the treatment of the condition exist, including the bisphosphonates, SERMs, and recombinant PTH. In addition, several new therapies are on the horizon. Estrogen replacement, which had in the past been recommended fairly universally to postmenopausal women, is now reserved for use in only very limited circumstances, based on studies that have demonstrated increases in certain cancers, stroke, and coronary artery disease [13; 76]. Prevention is critical, and patients should learn about diet, exercise, and medication use.

Finally, physicians and other providers should develop a greater understanding of osteoporosis and be more aggressive in addressing this topic. It is a disease that is increasing in prevalence and has significant morbidity, but also may often be treated with some success. Preventive measures should be discussed with patients earlier in life and not delayed until a patient is elderly.

RESOURCES

American Bone Health
https://americanbonehealth.org

International Osteoporosis Foundation
https://www.osteoporosis.foundation

Bone Health and Osteoporosis Foundation
https://www.bonehealthandosteoporosis.org

Osteoporosis Canada
https://osteoporosis.ca

The NIH Osteoporosis and Related Bone Diseases National Resource Center
https://www.niams.nih.gov/health-topics/bone-health-and-osteoporosis

FACULTY BIOGRAPHY

John J. Whyte, MD, MPH, is currently the Chief Medical Officer at WebMD. In this role, he leads efforts to develop and expand strategic partnerships that create meaningful change around important and timely public health issues. Previously, Dr. Whyte was the Director of Professional Affairs and Stakeholder Engagement at the FDA's Center for Drug Evaluation and Research and the Chief Medical Expert and Vice President, Health and Medical Education at Discovery Channel, part of the media conglomerate Discovery Communications.

Prior to this, Dr. Whyte was in the Immediate Office of the Director at the Agency for Healthcare Research Quality. He served as Medical Advisor/Director of the Council on Private Sector Initiatives to Improve the Safety, Security, and Quality of Healthcare. Prior to this assignment, Dr. Whyte was the Acting Director, Division of Medical Items and Devices in the Coverage and Analysis Group in the Centers for Medicare & Medicaid Services (CMS). CMS is the federal agency responsible for administering the Medicare and Medicaid programs. In his role at CMS, Dr.Whyte made recommendations as to whether or not the Medicare program should pay for certain procedures, equipment, or services. His division was responsible for durable medical equipment, orthotics/prosthetics, drugs/biologics/therapeutics, medical items, laboratory tests, and non-implantable devices. As Division Director as well as Medical Officer/Senior Advisor, Dr. Whyte was responsible for more national coverage decisions than any other CMS staff.

Dr. Whyte is a board-certified internist. He completed an internal medicine residency at Duke University Medical Center as well as earned a Master's of Public Health (MPH) in Health Policy and Management at Harvard University School of Public Health. Prior to arriving in Washington, Dr. Whyte was a health services research fellow at Stanford and attending physician in the Department of Medicine. He has written extensively in the medical and lay press on health policy issues.

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