Osteoporosis management: Use a goal-oriented, individualized approach

Recommendations for care are evolving, with increasingly sophisticated screening and diagnostic tools and a broadening array of treatment options.

**PRACTICE RECOMMENDATIONS**

- Consider screening for osteoporosis, using bone mineral density (BMD) by dual-energy X-ray absorptiometry (DXA), in all postmenopausal women ≥ 65 years and in women < 65 years at high risk of osteoporosis. **A**

- Consider screening in men ≥ 70 years and in younger men at high risk of fracture. **C**

- Use the trabecular bone score with DXA BMD to screen patients at high risk of fracture who have a normal BMD—eg, patients with type 2 diabetes or ankylosing spondylitis. **C**

- Offer individualized pharmacotherapy to older patients with a diagnosis of osteoporosis and to those at high risk of fracture. **A**

**Strength of recommendation (SOR)**

- Good-quality patient-oriented evidence **A**
- Inconsistent or limited-quality patient-oriented evidence **B**
- Consensus, usual practice, opinion, disease-oriented evidence, case series **C**

As the population of older adults rises, primary osteoporosis has become a problem of public health significance, resulting in more than 2 million fractures and $19 billion in related costs annually in the United States.\(^1\)

Despite the availability of effective primary and secondary preventive measures, many older adults do not receive adequate information on bone health from their primary care provider.\(^2\) Initiation of osteoporosis treatment is low even among patients who have had an osteoporotic fracture: Fewer than one-quarter of older adults with hip fracture have begun taking osteoporosis medication within 12 months of hospital discharge.\(^3\)

In this overview of osteoporosis care, we provide information on how to evaluate and manage older adults in primary care settings who are at risk of, or have been given a diagnosis of, primary osteoporosis. The guidance that we offer reflects the most recent updates and recommendations by relevant professional societies.\(^1,4-7\)

The nature and scope of an urgent problem

Osteoporosis is a skeletal disorder characterized by low bone mass and deterioration of bone structure that causes bone fragility and increases the risk of fracture.\(^8\) Operationally, it is defined by the World Health Organization as a bone mineral density (BMD) score below 2.5 SD from the mean value for a young White woman (ie, T-score ≤ –2.5).\(^9\) Primary osteoporosis is age related and occurs mostly in postmenopausal women and older men, affecting 25% of women and 5% of men ≥ 65 years.\(^10\)

An osteoporotic fracture is particularly devastating in an older adult because it can cause pain, reduced mobil-
The National Osteoporosis Foundation estimates that 20% of older adults who sustain a hip fracture die within 1 year due to complications of the fracture itself or surgical repair. Therefore, it is of paramount importance to identify patients who are at increased risk of fracture and intervene early.

**Clinical manifestations**

Osteoporosis does not have a primary presentation; rather, disease manifests clinically when a patient develops complications. Often, a fragility fracture is the first sign in an older person.

A fracture is the most important complication of osteoporosis and can result from low-trauma injury or a fall from standing height—thus, the term “fragility fracture.” Osteoporotic fractures commonly involve the vertebra, hip, and wrist. Hip and extremity fractures can result in limited or lost mobility and depression. Vertebral fractures can be asymptomatic or result in kyphosis and loss of height. Fractures can give rise to pain.

**Age and female sex are risk factors**

**TABLE 1,6,10** lists risk factors associated with osteoporosis. Age is the most important; prevalence of osteoporosis increases with age. Other nonmodifiable risk factors include female sex (the disease appears earlier in women who enter menopause prematurely), family history of osteoporosis, and race and ethnicity. Twenty percent of Asian and non-Hispanic White women > 50 years have osteoporosis.1 A study showed that Mexican Americans are at higher risk of osteoporosis than non-Hispanic Whites; non-Hispanic Blacks are least affected.10

Other risk factors include low body weight (< 127 lb) and a history of fractures after age 50. Behavioral risk factors include smoking, excessive alcohol intake (> 3 drinks/d), poor nutrition, and a sedentary lifestyle.1,6

**Who should be screened?**

Screening is generally performed with a clinical evaluation and a dual-energy x-ray absorptiometry (DXA) scan of BMD. Measurement of BMD is generally recommended for screening all women ≥ 65 years and those < 65 years whose 10-year risk of fracture is equivalent to that of a 65-year-old White woman (see “Assessment of fracture risk” later in the article). For men, the US Preventive Services Task Force recommends screening those with a prior fracture or a secondary risk factor for disease.2 However, the National Osteoporosis Foundation recommends screening all men ≥ 70 years and those 50 to 69 years whose risk profile shows heightened risk.1,4

DXA of the spine and hip is preferred; the distal one-third of the radius (termed “33% radius”) of the nondominant arm can be used when spine and hip BMD cannot be interpreted because of bone changes from the disease process or artifacts, or in certain diseases in which the wrist region shows the earliest change (eg, primary hyperparathyroidism).6,7

Clinical evaluation includes a detailed history, physical examination, laboratory screening, and assessment for risk of fracture.

**History.** Explore the presence of risk factors, including fractures in adulthood, falls, medication use, alcohol and tobacco use, family history of osteoporosis, and chronic disease.

**Physical exam.** Assess height, including any loss (> 1.5 in) since the patient’s second or third decade of life; kyphosis; frailty; and balance and mobility problems.

**Laboratory and imaging studies.** Perform basic laboratory testing when DXA is abnormal, including thyroid function, serum
Pharmacotherapy is recommended in all cases of osteoporosis and osteopenia when risk of fracture is high. Oral bisphosphonates can be used as initial treatment.
we recommend the following strategies; take each patient’s individual situation into consideration when electing to adopt any of these measures.

Vitamin D. Consider checking the serum 25-hydroxyvitamin D level and providing supplementation (800-1000 IU daily, the National Osteoporosis Foundation recommends1) as necessary to maintain the level at 30-50 ng/mL.6

Calcium. Encourage a daily dietary calcium intake of 1000-1200 mg. Supplement calcium if you determine that diet does not provide an adequate amount.

Alcohol. Advise patients to limit consumption to < 3 drinks a day.

Tobacco. Advise smoking cessation.

Activity. Encourage an active lifestyle, including regular weight-bearing and balance exercises and resistance exercises such as Pilates, weightlifting, and tai chi. The regimen should be tailored to the patient’s individual situation.

Medical therapy for concomitant illness. When possible, prescribe medications for chronic comorbidities that can also benefit bone health. For example, long-term use of angiotensin-converting enzyme (ACE) inhibitors and thiazide diuretics for hypertension are associated with a slower decline in BMD in some populations.21-23

Tailor treatment to patient’s circumstances

TABLE 2

<table>
<thead>
<tr>
<th>Measures to prevent osteoporosis1,6</th>
</tr>
</thead>
<tbody>
<tr>
<td>Avoid smoking</td>
</tr>
<tr>
<td>Reduce alcohol intake</td>
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<tr>
<td>Increase physical activity, including a regular regimen of weight-bearing exercises</td>
</tr>
<tr>
<td>Maintain a blood level of 25-hydroxyvitamin D of ≥ 30 ng/mL (75 nmoL/L)</td>
</tr>
<tr>
<td>Ensure adequate intake of calcium (1000-1200 mg/d)</td>
</tr>
</tbody>
</table>

values and preferences, to come to a shared decision. Tailoring treatment, based on the patient’s distinctive circumstances, through shared decision-making is key to compliance.25

Pharmacotherapy is not indicated in patients whose risk of fracture is low; however, you should reassess such patients every 2 to 4 years.26 Women with a very high BMD might not need to be restested with DXA any sooner than every 10 to 15 years.

There are 3 main classes of first-line pharmacotherapeutic agents for osteoporosis in older adults (TABLE 44,6,7,26-41): antiresorptives (bisphosphonates and denosumab), anabolics (teriparatide and abaloparatide), and a monoclonal sclerostin antibody (romosozumab). (TABLE 44,6,7,26-41 and the discussion in this section also remark on the selective estrogen-receptor modulator raloxifene, which is used in special clinical circumstances but has been removed from the first line of osteoporosis pharmacotherapy.)

Bisphosphonates. Oral bisphosphonates (alendronate, ibandronate, risedronate) can be used as initial treatment in patients with a high risk of fracture.35 Bisphosphonates have been shown to reduce fracture risk and improve BMD. When an oral bisphosphonate cannot be tolerated, intravenous zoledronate or ibandronate can be used.41

Patients treated with a bisphosphonate should be assessed for their fracture risk after 3 to 5 years of treatment; when intravenous zoledronate is given as initial therapy, patients should be assessed after 3 years. After assessment, patients who remain at high risk should continue treatment; those whose fracture risk has decreased to low or moderate should have treatment temporarily suspended (bisphosphonate holiday) for as long as 5 years.26 Patients on bisphosphonate holiday should have their fracture risk assessed at 2- to 4-year intervals.26 Restart treatment if there is an increase in fracture risk (eg, a decrease in BMD) or if a fracture occurs. Bisphosphonates have a prolonged effect on BMD—for many years after treatment is discontinued.27,28

Oral bisphosphonates are associated with gastroesophageal reflux disease, difficulty swallowing, and gastritis. Rare adverse effects include osteonecrosis of the jaw and...
atypical femur fracture.  

**Denosumab**, a recombinant human antibody, is a relatively newer antiresorptive for initial treatment. Denosumab, 60 mg, is given subcutaneously every 6 months. The drug can be used when bisphosphonates are contraindicated, the patient finds the bisphosphate dosing regimen difficult to follow, or the patient is unresponsive to bisphosphonates. 

Patients taking denosumab are reassessed every 5 to 10 years to determine whether to continue therapy or change to a new drug. Abrupt discontinuation of therapy can lead to rebound bone loss and increased risk of fracture. As with bisphosphonates, long-term use can be associated with osteonecrosis of the jaw and atypical femur fracture. 

There is no recommendation for a drug holiday for denosumab. An increase in, or no loss of, bone density and no new fractures while being treated are signs of effective treatment. There is no guideline for stopping denosumab, unless the patient develops adverse effects.

**Bone anabolics.** Patients with a very high risk of fracture (eg, who have sustained multiple vertebral fractures), can begin treatment with teriparatide (20 μg/d subcutaneously) or abaloparatide (80 μg/d subcutaneously) for as long as 2 years, followed by treatment with an antiresorptive, such as a bisphosphonate. Teriparatide can be used in patients who have not responded to an antiresorptive as first-line treatment.

Both abaloparatide and teriparatide might be associated with a risk of osteosarcoma and are contraindicated in patients who are at increased risk of osteosarcoma. 

**Romosozumab**, a monoclonal sclerostin antibody, can be used in patients with very high risk of fracture or with multiple vertebral fractures. Romosozumab increases bone formation and reduces bone resorption. It is given monthly, 210 mg subcutaneously, for 1 year. The recommendation is that patients who have completed a course of romosozumab continue with antiresorptive treatment. 

Romosozumab is associated with an increase in the risk of cardiovascular disease, including stroke and myocardial infarction.

**Raloxifene**, a selective estrogen-receptor modulator, is no longer a first-line agent for osteoporosis in older adults because of its association with an increased risk of deep-vein thrombosis, pulmonary embolism, and lethal stroke. However, raloxifene can be used, at 60 mg/d, when bisphosphonates or denosumab are unsuitable. In addition, raloxifene is particularly useful in women with a high risk of breast cancer and in men who are taking a long-acting gonadotropin-releasing hormone agonist for prostate cancer.

### Influence of chronic disease on bone health

Chronic diseases—hypertension, type 2 diabetes, hyperthyroidism, rheumatoid arthritis, ankylosing spondylitis, and gastroenterologic disorders such as celiac disease and ulcerative colitis—are known to affect bone loss that can hasten osteoporosis. Furthermore, medications used to treat chronic diseases are known to affect bone health: Some, such as statins, ACE inhibitors, and hydrochlorothiazide, are bone protective; others, such as steroids, pioglitazone, and selective serotonin reuptake inhibitors, accelerate bone loss. It is important to be aware of the effect of a patient’s chronic diseases.
and treatments for those diseases, on bone health, to help develop an individualized osteoporosis prevention plan.

**Monitoring the efficacy of treatment**

Treatment of osteoporosis should not be initiated without baseline measurement of BMD of the spine and hip. Subsequent to establishing that baseline, serial measurement of BMD can be used to (1) determine when treatment needs to be initiated for an untreated patient and (2) assess response in a treated patient. There is no consensus on the interval at which DXA should be repeated for the purpose of monitoring treatment response;

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**TABLE 4**

Pharmacotherapy for age-related osteoporosis 4,6,7,26-41

<table>
<thead>
<tr>
<th>Medication</th>
<th>Dosage and route</th>
<th>Comments, cautions, and cost</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>ANTIRESORPTIVE AGENTS</strong></td>
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| Bisphosphonates | Older patients are not ideal candidates for an oral bisphosphonate if they have either  
  • dementia (and do not have help with medication management or cannot follow instructions for taking medication)  
  or  
  • dysphagia  
  **Caution**: Avoid bisphosphonates in patients with severe renal disease (ie, glomerular filtration rate < 30 mL/min) | |
| ![](image)

- **Alendronate**  
  10 mg/d orally  
  Not a common dosing option  
  Using a different formulation (oral solution or effervescent tablet) might improve adherence and reduce the risk of gastrointestinal adverse effects  
  70 mg/wk orally  
  Typically given to patients who do not have gastroesophageal reflux disease, gastritis, or esophagitis  
  **Caution**: Preference is to not give to patients who have polypharmacy and need to take an early-morning medication before breakfast (eg, thyroid medication)  
  70-mg tablet: $10.23 |
| ![](image)

- **Ibandronate**  
  150 mg once monthly orally  
  Compared to placebo, significantly reduces the risk of vertebral fracture  
  Monthly tablet might be a good choice for patients who have difficulty taking multiple pills per day  
  150-mg tablet: $14.13 |
| ![](image)

- **Risedronate**  
  5 mg/d, 35 mg/wk, or  
  150 mg/mo orally  
  Monthly regimen is preferred, especially for patients with polypharmacy or difficulty swallowing a pill  
  150-mg tablet: $50.85 |
| ![](image)

- **Zoledronate**  
  5 mg IV once/ly  
  Valuable for patients who cannot tolerate an oral medication and are therefore at risk of nonadherence  
  Suitable when all these criteria apply:  
  • good kidney function  
  • able to travel to a transfusion center  
  • can tolerate an hour-long infusion  
  • not expected to have invasive dental work, such as tooth extraction, performed for 1 year after infusion  
  5 mg/100 mL dose: $240.40 |
| ![](image)
### TABLE 4
Pharmacotherapy for age-related osteoporosis (cont’d)

<table>
<thead>
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</table>
| Denosumab   | 60 mg every 6 mo subcutaneously | Good option for patients who  
  - cannot manage medication without assistance  
  or  
  - have difficulty swallowing a pill or following instruction (eg, cognitively impaired)  
  Requires that patients  
  - travel to a clinic for administration every 6 mo  
  or  
  - live in a facility where the medication can be delivered to them  
  Treatment of choice for patients with end-stage renal disease; it is important to collaborate with the nephrologist to manage calcium, vitamin D, and parathyroid hormone levels in end-stage renal disease patients  
  1 mL of a 60-mg solution: $990 |

| **BONE ANABOLICS** |             |                               |
| Teriparatide | 20 μg/d subcutaneously | Suitable when any of these criteria apply:  
  - already tried an antiresorptive agent  
  - severely suppressed bone-turnover markers  
  - nonunion or delayed healing of fracture  
  **Caution:** Contraindicated in patients  
  - at increased risk of bone cancer (eg, with Paget disease of bone or a history of radiation therapy of the skeleton)  
  or  
  - with bone metastases, hypercalcemia, or bone malignancy  
  **Caution:** Associated with an increased incidence of osteosarcoma in a rat model; however, in a recent human observational study with 15-year surveillance, no difference was seen in the incidence of teriparatide-associated osteosarcoma between patients treated with teriparatide for 2 years and those who were not treated with teriparatide  
  1-month supply: $3,359 |

Frequency depends on the individual's circumstances and the medication used. Notably, many physicians repeat DXA after 2 years of treatment; however, the American College of Physicians recommends against repeating DXA within the first 5 years of pharmacotherapy in women.

Patients with suspected vertebral fracture or those with loss of height > 1.5 inches require lateral radiographs of the thoracic and lumbar spine to assess the status of fractures.

**Bone-turnover markers** measured in serum can be used to assess treatment efficacy and patient adherence. The formation marker procollagen type I N-terminal propeptide (P1NP) and the resorption marker beta C-terminal cross-linking telopeptide of type 1 collagen (bCTX) are preferred for evaluating bone turnover in the clinical setting. Assessing P1NP and bCTX at baseline...
and after 3 months of treatment might be effective in monitoring adherence, particularly in patients taking a bisphosphonate.44

Be sure to address fall prevention
It is important to address falls, and how to prevent them, in patients with osteoporosis. Falls can precipitate fracture in older adults with reduced BMD, and fractures are the most common and debilitating manifestation of osteoporosis. Your discussion of falls with patients should include45:
• consequences of falls
• cautions about medications that can cloud mental alertness
• use of appropriate footwear
• home safety, such as adequate lighting, removal of floor clutter, and installation of handrails in the bathroom and stairwells and on outside steps.
• having an annual comprehensive eye exam.

Osteoporosis is avoidable and treatable
Earlier research reported various expressions of number needed to treat for medical management of osteoporosis—making it difficult to follow a single number as a reference for gauging the effectiveness of pharmacotherapy.46,47 However, for older adults of different ethnic and racial backgrounds with multiple comorbidities and polypharmacy, it might be more pragmatic in primary care to establish a model of goal-oriented, individualized care.

### TABLE 4

Table: Pharmacotherapy for age-related osteoporosis4,6,7,26-41 (cont’d)

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<td><strong>BONE ANABOLICS</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Abaloparatide</td>
<td>80 μg/d subcutaneously</td>
<td>Suitable when any of these patient criteria apply:</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• already tried an antiresorptive agent</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• have severely suppressed bone-turnover markers</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• have nonunion or delayed healing of fractures</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Medication does not need to be refrigerated, which is advantageous for patients who travel frequently or live where refrigeration is unavailable</td>
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<tr>
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<tr>
<td></td>
<td></td>
<td>1-month supply: $1,768</td>
</tr>
<tr>
<td><strong>MONOCLONAL SCLEROSTIN ANTIBODY</strong></td>
<td></td>
<td>Use raises concern when the patient has a history of stroke</td>
</tr>
<tr>
<td>Romosozumab</td>
<td>210 mg subcutaneously as a single dose monthly</td>
<td>1 injection: $1,825</td>
</tr>
<tr>
<td><strong>SELECTIVE ESTROGEN-RECEPTOR MODULATOR</strong></td>
<td></td>
<td>A reduced risk of vertebral fracture with raloxifene was documented in clinical trials; evidence of a reduction in hip fracture risk is lacking, however</td>
</tr>
<tr>
<td>Raloxifene</td>
<td>60 mg/d orally</td>
<td>Can be used as a second-line agent</td>
</tr>
<tr>
<td></td>
<td></td>
<td><strong>Caution</strong>: Presents a risk of deep vein thrombosis</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1-month supply: $96</td>
</tr>
</tbody>
</table>

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By focusing on prevention of bone loss, and being mindful that the risk of fracture almost doubles with a decrease of 1 SD in BMD, you can translate numbers to goals of care.\textsuperscript{48}

In the United States, approximately one-half of osteoporosis cases in adults $\geq$ 50 years are managed by primary care providers. As a chronic disease, osteoporosis requires that you, first, provide regular monitoring and assessment, because risk can vary with comorbidities,\textsuperscript{49} and, second, discuss and initiate screening and treatment as appropriate, which can be done annually during a well-care visit.

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References


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