This is a corrected version of the Practice Guidelines that appeared in print.

ACP Releases Guideline on Treatment of Low Bone Mineral Density or Osteoporosis to Prevent Fractures

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More than one half of persons 50 years and older are affected by osteoporosis, and an additional 34 million persons in the United States have an increased risk of osteoporosis because of low bone mass. The hip, spine, and wrist are most likely to be affected. The occurrence of fragility fractures and the finding of low bone mineral density (BMD) help to diagnose osteoporosis. The first-line test for diagnosis is dual x-ray absorptiometry (DEXA). Femoral neck BMD of 2.5 or more standard deviations below the mean is the international reference standard for diagnosis of osteoporosis in postmenopausal women and in men 50 years and older. Low BMD, as measured by DEXA, does not perfectly predict fracture risk. Less than one half of persons who eventually have an osteoporotic fracture are identified by DEXA as having low BMD. Guidelines for screening for osteoporosis in women are well established, and the American College of Physicians (ACP) recently released a guideline for men. This ACP guideline on treatment of low BMD or osteoporosis to prevent fractures describes the available evidence on pharmacologic treatment in men and women.

Bisphosphonates, including alendronate (Fosamax), zoledronic acid (Reclast), and risedronate (Actonel), have been shown to reduce vertebral, nonvertebral, and hip fracture risk. Etidronate (Didronel) and ibandronate (Boniva) have been shown to reduce vertebral fracture risk. Ibandronate (Boniva) has been shown to reduce vertebral fracture risk. The optimal duration of treatment is unclear, but studies on bisphosphonates have lasted three to 60 months. Estrogen reduces vertebral, nonvertebral, and hip fracture risk. It is unclear if calcium reduces fracture risk; however, evidence is stronger for combined calcium and vitamin D than for calcium alone. Data have shown that there is a statistically significant reduction in vertebral fractures with vitamin D analogues, but results are mixed for nonvertebral and hip fractures.

Oral bisphosphonates are associated with gastrointestinal adverse effects, including acid reflux. Pooled analyses have shown no difference in mild upper gastrointestinal effects among alendronate, ibandronate, risedronate, or zoledronic acid compared with placebo. Raloxifene (Evista) increases the risk of pulmonary embolism and thromboembolic events, and estrogen appears to increase the risk of cerebrovascular and thromboembolic events.

Recommendations

Physicians should offer pharmacologic treatment to men and women with osteoporosis or fragility fractures. There is good evidence to support treating persons with osteoporosis to prevent continued bone loss and reduce the risk of fracture. Randomized controlled trials have shown that, compared with placebo, alendronate, ibandronate, risedronate, calcitonin (Miacalcin), teriparatide (Forteo), and raloxifene prevent vertebral fractures; teriparatide prevents nonvertebral fractures; and risedronate and alendronate prevent nonvertebral and hip fractures. Estrogen has been shown to reduce vertebral, nonvertebral, and hip fractures. The evidence on calcium alone or in combination with vitamin D is mixed. Most trials use calcium and vitamin D; therefore, they should be added to treatment regimens. Optimal duration of treatment is unknown.

Physicians should consider pharmacologic treatment for men and women at risk of osteoporosis. Persons at risk of osteoporosis, but who do not have a T-score lower than –2.5 should be given treatment. Data supporting preventive treatment are stronger for persons at moderate risk of osteoporosis (i.e., persons with a T-score of –1.5 to –2.5, those receiving glucocorticoids, or those older than 62 years). ▶

Table 1. Summary of Evidence About Drugs and Fracture Risk

	Effect on fracture risk (level of evidence)				
Agent	*Vertebral*	*Nonvertebral*	*Hip*	*Adverse effects*	*FDA approval*
Bisphosphonates					
Alendronate (Fosamax)	Decreased (strong)	Decreased (strong)	Decreased (strong)	Mild upper GI events, esophageal ulcerations, perforations, bleeding events	Prevention or treatment
Etidronate (Didronel)	Decreased (strong)	No effect (fair)	No effect (strong)	Mild upper GI events, esophageal ulcerations, perforations, bleeding events	Not approved for prevention or treatment
Ibandronate (Boniva)	Decreased (strong)	No effect (strong)	Not studied	Esophageal ulcerations, perforations, bleeding events	Prevention or treatment
Pamidronate (Aredia)	No effect (weak)	No effect (weak)	No effect (weak)	Mild upper GI events, esophageal ulcerations, perforations, bleeding events	Not approved for prevention or treatment
Risedronate (Actonel)	Decreased (strong)	Decreased (strong)	Decreased (strong)	Esophageal ulcerations, perforations, bleeding events	Prevention or treatment
Zoledronic acid (Reclast)	Decreased (strong)	Decreased (strong)	Decreased (strong)	Muscular and joint pain	Prevention
Calcitonin (Miacalcin)	Decreased (fair)	No effect (strong)	Not studied	No clinically significant adverse effects	Treatment
Calcium and vitamin D	Modest effect* (strong)	Modest effect* (strong)	Modest effect* (strong)	No clinically significant adverse effects	Over the counter
Estrogen	Decreased (strong)	Decreased (strong)	Decreased (strong)	Thromboembolic events; cerebrovascular accident, stroke, and breast cancer (when combined with progestin); gynecologic problems (endometrial bleeding); breast abnormalities (pain, tenderness, fibrocytosis)	Prevention
Selective estrogen receptor modulators					
Raloxifene (Evista)	Decreased (strong)	No effect (strong)	No effect (strong)	Pulmonary embolism, thromboembolic events	Prevention or treatment
Tamoxifen (formerly Nolvadex)	No effect (strong)	Not studied	No effect (strong)	Pulmonary embolism	Not approved for prevention or treatment
Teriparatide (Forteo)	Decreased (strong)	Decreased (fair)	No effect (weak)	No clinically significant adverse effects	Treatment
Testosterone	Not studied	Not studied	Not studied	No clinically significant adverse effects	Not approved for prevention or treatment

FDA = U.S. Food and Drug Administration; GI = gastrointestinal.

**—Pooled estimate across fracture sites.*

Adapted with permission from Qaseem A, Snow V, Shekelle P, Hopkins R Jr., Forciea MA, Owens DK, for the Clinical Efficacy Assessment Subcommittee of the American College of Physicians. Pharmacologic treatment of low bone density or osteoporosis to prevent fractures: a clinical practice guideline from the American College of Physicians. Ann Intern Med. *2008;149(6):410.*

Osteoporosis risk is increased in men older than 70 years, those with a body mass index less than 20 to 25 kg per m^2, those with weight loss in recent years, and those with weight loss of more than 10 percent compared with usual young or adult weight. It is also increased in men who are physically inactive, who are taking corticosteroids, and who are on androgen deprivation therapy. Risk is increased in women with lower body weight, and in those who smoke, have lost weight, have a family history of osteoporosis, have decreased physical activity, use alcohol or caffeine, and have low calcium and vitamin D intake.

Physicians should choose pharmacologic treatment options based on risks and benefits for individual

persons, as well as adverse effects *(Table 1)*. Evidence has shown that bisphosphonates are a reasonable first-line treatment option, especially in persons at high risk of hip fracture. There is insufficient evidence to show that one bisphosphonate is better than another. Alendronate and risedronate are the most studied bisphosphonates. Ibandronate has not been shown to reduce nonvertebral or hip fractures. Zoledronic acid in persons with recent hip fracture reduced subsequent fracture and improved survival rates.

Although estrogen is effective in preventing vertebral, nonvertebral, and hip fractures, it is associated with serious risks. Calcitonin does not appear to reduce nonvertebral and hip fractures. Calcium and vitamin D are used as part of the treatment regimen in most studies of pharmacologic therapy for osteoporosis.

Gastrointestinal adverse effects are common with bisphosphonates. No evidence exists regarding the risk of serious cardiac events with bisphosphonates, calcium, vitamin D, calcitonin, or teriparatide. Etidronate increases the risk of esophageal ulcers, bleeding events, and mild upper gastrointestinal events. Raloxifene is associated with a higher risk of pulmonary embolism, thromboembolic events, and mild cardiac events. Estrogen increases the risk of stroke, and estrogen/progestin increases the risk of stroke and breast cancer. All bisphosphonates except zoledronic acid are associated with perforations, ulcerations, and bleeding events.

More research on osteoporosis treatment in men and women should be done. Current evidence focuses on postmenopausal women; more information is needed on other populations, including men. Head-to-head studies powered to determine differences in effectiveness of various medications would be helpful, as would information on bisphosphonates and osteonecrosis of the jaw; prevention strategies; and treatment duration. ■

Answers to This Issue's CME Quiz

Q1. C
Q2. B
Q3. C
Q4. D
Q5. D
Q6. D
Q7. C
Q8. A, B, C, D
Q9. A, B, C, D
Q10. B, C, D