

AMERICAN ASSOCIATION OF CLINICAL ENDOCRINOLOGISTS | AMERICAN COLLEGE OF ENDOCRINOLOGY

Male Osteoporosis

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Osteoporosis Affects Men Too

- Osteoporosis is an often asymptomatic disorder characterized by decreased bone strength and increased risk for bone fractures. Osteoporosis is less common in men than women, but it still affects a significant number of men. Of the 44 million Americans who have either osteoporosis or low bone mineral density (BMD), approximately 20%—more than 8 million—are men.

NIH Consensus Development Panel on Osteoporosis Prevention, Diagnosis, and Therapy. Osteoporosis prevention, diagnosis, and therapy. *JAMA* 2001; 285:785–795.

Burge R et al. Incidence and economic burden of osteoporosis-related fractures in the United States. *J Bone Miner Res* 2007; 22:465–475.

Nelson B et al. Osteoporosis in men: an endocrine society clinical practice guideline. *J Clin Endocrinol Metab* 2012; 97:1802-1822.

The Burden of Osteoporosis in Men

- Men are also at significant risk for fractures due to osteoporosis. Approximately 30% to 40% of osteoporosis-related fractures occur in men. In males 50 and older, the lifetime risk of fracture is as high as 30%.
- In addition, men with hip fractures have a mortality rate two to three times higher than women. The mortality rate after a vertebral fracture is also significantly higher in men.

Bliuc D et al. Mortality risk associated with low-trauma osteoporotic fracture and subsequent fracture in men and women. *JAMA* 2009 301: 513–521.

Haentjens P et al. Meta-analysis: excess mortality after hip fracture among older women and men. *Ann Intern Med* 2010; 152:380–390.

Center JR et al. Mortality after all major types of osteoporotic fracture in men and women: an observational study. *Lancet*. 1999;353(9156):878-82.

Men Are Often Overlooked

- Despite the substantial clinical burden of osteoporosis, the condition is commonly under-diagnosed and under-treated, especially in men.
- In one study of men and women 50 and older who were hospitalized for fragility hip fractures, only 4.5% of men were receiving any kind of osteoporosis treatment at discharge, compared with 27% of women. At 1 to 5 years of follow-up, only 11% of men had a BMD measurement, compared with 27% of women.
- In another, similar study of men and women with osteoporosis-related fractures, the vast majority of men (more than 95%) and more than half the women (51%) were not evaluated or treated according to current guideline or expert recommendations.

Kiebzak GM et al. Under-treatment of osteoporosis in men with hip fracture. *Arch Intern Med.* 2002;162:2217-22.

Feldstein A et al. Bone mineral density measurement and treatment for osteoporosis in older individuals with fractures: a gap in evidence-based practice guideline implementation.

Arch Intern Med. 2003;163:2165-72.

A Silent Disease

- Osteoporosis is typically asymptomatic. The first clinical manifestation of the condition is usually a fracture. Of the 3.5 million fractures that occurred in men worldwide in 2000, 16% were at the vertebrae; 14% at the hip; 10% at the forearm; 5% at the humerus; and 55% at other sites including the pelvis, tibia, fibula, ribs, clavicle, scapula, and sternum.
- Even vertebral fractures can be asymptomatic. They are often diagnosed as incidental findings on chest or abdominal radiographs. However, back pain, loss of height, and a stooped posture can be symptoms of a vertebral fracture.

Johnell O, Kanis JA. An estimate of the worldwide prevalence and disability associated with osteoporotic fractures. *Osteoporos Int* 2006; 17:1726–1733.

Mayo Clinic. Osteoporosis: Symptoms & Causes. Available at <https://www.mayoclinic.org/diseases-conditions/osteoporosis/symptoms-causes/syc-20351968>. Accessed August 14, 2018.

Who Should Be Tested?

- The Endocrine Society recommends BMD testing in all men 70 or older.
- Men age 50-69 should be tested if they have a history of fracture or other risk factors including the following:
 - Delayed puberty
 - Hypogonadism
 - Hyperparathyroidism
 - Hyperthyroidism
 - Chronic obstructive pulmonary disease
 - Use of glucocorticoids or GnRH agonists
 - Alcohol abuse or smoking

Diagnosing Osteoporosis in Men

- The Endocrine Society and National Osteoporosis Foundation recommend the following men be diagnosed with osteoporosis and receive treatment.
 - Men who have had a hip or vertebral fracture without major trauma (fragility fracture).
 - Men who have not experienced a spine or hip fracture but whose BMD T-score of the spine, femoral neck, and/or total hip is -2.5 .
 - Men with a T-score between -1.0 and -2.5 in the spine, femoral neck, or total hip (low bone mass) if the 10-year risk for any fracture is $\geq 20\%$ or the 10-year risk of hip fracture is $\geq 3\%$ using the FRAX risk calculator. (Available at: <https://www.sheffield.ac.uk/FRAX/>)

Lifestyle Recommendations for Men with Osteoporosis

- Stop smoking and reduce alcohol intake to less than three drinks per day.
- Participate in weight-bearing activities for 30–40 min per session, three to four sessions per week.
- Consume 1,000–1,200 mg calcium daily, ideally from dietary sources, with calcium supplements added if dietary calcium is insufficient.
- If vitamin D levels are low (<30 ng/ml), take vitamin D supplements to achieve blood 25(OH)D levels of at least 30 ng/ml.

Pharmacologic Therapy for Men with Osteoporosis

- FDA-approved drugs for treating men with osteoporosis:
 - Bisphosphonates: alendronate, risedronate, and zoledronic acid (ibandronate is not approved for men)
 - Denosumab: a human monoclonal anti-RANK ligand antibody (for men with osteoporosis or receiving ADT for prostate cancer)
 - Teriparatide: recombinant human parathyroid hormone 1-34

Khosla S and Hofbauer LC. Osteoporosis treatment: recent developments and ongoing challenges. *Lancet Diabetes Endocrinol* 2017; 5:898-907.

National Osteoporosis Foundation. Medication and Treatment Adherence: The How's and Why's of Osteoporosis Medications. Available at:

<https://www.nof.org/patients/treatment/medicationadherence/>. Accessed August 15, 2018.

Watts, NB et al. Osteoporosis in men: an endocrine society clinical practice guideline. *J Clin Endocrinol Metab* 2012; 97:1802-1822.

Which Agent?

- Select the most appropriate agent for individual patients based on:
 - Fracture history
 - Severity of osteoporosis
 - Comorbidities (peptic ulcer disease, gastroesophageal reflux, malabsorption syndromes, malignancy)
 - Cost

Key Recommendations for Selecting the Best Agent

- For most men, the generic oral bisphosphonates alendronate or risedronate may be used as initial agents because of extensive experience with their use, lack of evidence that other agents are more effective, and low cost.
- For men with upper or lower gastrointestinal problems, a non-oral therapy such as zoledronic acid, denosumab, or teriparatide may be preferred.
- In men with a recent hip fracture, zoledronic acid is recommended. Clinical evidence shows zoledronic acid can reduced risk of recurrent hip fractures.

Key Recommendations, continued

- For men at high risk of vertebral fracture, teriparatide may be preferred because it increases spine BMD more than alendronate, although it is more expensive. Teriparatide or denosumab could also be considered for men who fail to tolerate or respond adequately to bisphosphonates.
- Oral bisphosphonates should be used with caution in men with impaired kidney function (estimated glomerular filtration rate [eGFR] ≤ 30 – 35 ml/min). Zoledronic acid is contraindicated in patients with eGFR < 35 ml/min. Potential safety concerns with bisphosphonates include osteonecrosis of the jaw and atypical femur fractures.

Monitoring Treatment

- Clinicians should monitor BMD by dual-energy x-ray absorptiometry at the spine and hip every 1-2 years to assess treatment response. If BMD reaches a plateau, the frequency of BMD measurements may be reduced.
- Consider measuring bone turnover 3–6 months after initiating treatment using a bone resorption marker, such as serum CTX or serum or urine NTX, for antiresorptive therapy and a bone formation marker such as serum PINP for anabolic therapy.