

## Osteoporosis in Men

**TO THE EDITOR:** In his review of osteoporosis in men, Ebeling (April 3 issue)<sup>1</sup> presents the World Health Organization (WHO) diagnostic criteria for osteoporosis. Since then, the WHO has developed an approach to determining risk, using data from large international cohorts. This is available online as a calculator, which gives the absolute risk of a hip fracture within the next decade, based on bone density and other clinical risk factors ([www.shef.ac.uk/FRAX/index.htm](http://www.shef.ac.uk/FRAX/index.htm)). The calculator requires input of a T score, which must be derived from the normal reference range for young women. However, in the United States, most of the bone-density reports give the T score based on the reference range for young men. Many physicians do not realize that they need to do an additional step to use the calculator for men. The mean ( $\pm$ SD) value for the femoral neck in young women is  $0.858 \pm 0.120$  g per square centimeter, and for young men it is  $0.934 \pm 0.137$  g per square centimeter.<sup>2</sup> To convert a male-referent T score (mT) into a female-referent T score (fT), the following equation should be used:

$$fT = \{[(mT \times 0.137) + 0.934] - 0.858\} \div 0.120.$$

Susan M. Ott, M.D.

University of Washington  
Seattle, WA 98195  
smott@u.washington.edu

1. Ebeling PR. Osteoporosis in men. *N Engl J Med* 2008;358:1474-82.
2. Looker AC, Wahner HW, Dunn WL, et al. Updated data on proximal femur bone mineral levels in US adults. *Osteoporos Int* 1998;8:468-89.

**TO THE EDITOR:** Ebeling describes vertebral-fracture reduction with the use of teriparatide in men<sup>1</sup>; however, the data in the cited study were partly based on treatment with the 40- $\mu$ g dosage, the fracture data were collected not only during but also after treatment with teriparatide, and the difference was found only for moderate-to-severe fractures. Relevant data for risedronate were not mentioned: among men after stroke, the risk of hip fracture was reduced (0.19; 95% confidence interval [CI], 0.04 to 0.89),<sup>2</sup> and among glucocorticoid-treated men, the risk of vertebral fracture decreased by 82% (95% CI, 37 to 95), as compared with placebo.<sup>3</sup>

Risedronate is registered in Europe for use in men, based on the results of a randomized, placebo-controlled trial, in which an increase in the

bone mineral density of the spine and hips was observed.<sup>4</sup> This seems reasonable, since studies with fractures as the primary end point are less feasible in men for economic reasons, and these drugs have been demonstrated to reduce the risk of fracture among women.

Willem F. Lems, M.D., Ph.D.

VU University Medical Center  
1007 MB Amsterdam, the Netherlands  
wf.lems@vumc.nl

Piet P.M.M. Geusens, M.D., Ph.D.

Maastricht University Medical Center  
6202 AZ, Maastricht, the Netherlands

Drs. Lems and Geusens report receiving lecture fees from Eli Lilly, Procter & Gamble, Merck, Roche, and Servier. No other potential conflict of interest relevant to this letter was reported.

1. Kaufman JM, Orwoll E, Goemaere S, et al. Teriparatide effects on vertebral fractures and bone mineral density in men with osteoporosis: treatment and discontinuation of therapy. *Osteoporos Int* 2005;16:510-6.
2. Sato Y, Iwamoto J, Kanoko T, Satoh K. Risedronate sodium therapy for prevention of hip fractures in men 65 years or older after stroke. *Arch Intern Med* 2005;165:1743-8.
3. Reid DM, Adami S, DeVogelaer JP, Chines AA. Risedronate increases bone mineral density and reduces vertebral fracture risk within one year in men on corticosteroid therapy. *Calcif Tissue Int* 2001;69:242-7.
4. Boonen S, Wenderoth D, Schofield PJ, Cahall D, Orwoll ES. Oral risedronate treatment in men with osteoporosis: study design and baseline characteristics. *J Bone Miner Res* 2005;20:Suppl 1:S282. abstract.

**TO THE EDITOR:** In regard to the use of bisphosphonates in men with osteoporosis, the studies cited do not seem to support either the published guidelines or the recommendations by Ebeling for the patient described in the vignette. One study showed a decrease only in radiologic — ergo asymptomatic — vertebral fractures. Another also showed a decrease only in radiologic vertebral fractures, and it was not blinded. A third study showed a decrease in clinical fractures, but not hip fractures, in men with a previous hip fracture.

For men with a low T score and no history of fractures or with a low score and only radiologic evidence of vertebral fractures, with or without other risk factors, what evidence exists to show that bisphosphonates will provide a benefit?

Mark Joy, M.D., J.D.

VA New York Harbor Healthcare System  
Brooklyn, NY 11209  
mark.joy@va.gov

**THE AUTHOR REPLIES:** I am grateful to Ott for her timely comments on using the WHO online calculator (FRAX) for assessing the absolute risk of a hip fracture within the next decade in men, based on femoral-neck bone density and other clinical risk factors.<sup>1</sup> This tool is mentioned in my review of osteoporosis in men, as is the calculation of male-referent T scores with the use of a reference range for young men rather than for young women. To use the online calculator in men, the male-referent T score should be converted into a female-referent T score with the use of the equation provided. Ideally, the FRAX tool could be updated to include an online formula for this conversion to be made before the derived female-referent T score is used in the absolute-fracture-risk calculator.

Lems and Geusens provide further evidence of the efficacy of risedronate and teriparatide treatment. Limited space in my article precluded a comprehensive review of the literature. The study of treatment with teriparatide in men with osteoporosis was terminated prematurely after an average follow-up of 11 months. Currently, treatment is recommended for a total of 18 to 24 months. The follow-up study data showing that vertebral fractures are reduced by teriparatide are reassuring and likely to be clinically relevant. The problem in assessing the efficacy of any treatment for osteoporosis in men is the lack of data from published trials using fractures as a primary end point. The studies referred to in my review and by

these authors examined fracture rates as secondary end points and had limited statistical power. Larger studies are required to definitively determine the effects of newer treatments on vertebral, nonvertebral, and hip fractures in men with osteoporosis. However, evidence of the efficacy of these drugs may be limited to data from studies using the surrogate end points of bone mineral density and bone-turnover markers, such as the study of risedronate in men with osteoporosis by Boonen et al.,<sup>2</sup> with generalization of antifracture efficacy from studies in postmenopausal women with osteoporosis.

Joy's questioning of the evidence on which current published guidelines or treatment recommendations are based reinforces the need for larger studies of treatment in men with osteoporosis. However, it makes sense to initiate treatment in men with the highest absolute risk of fracture, since they will be most likely to benefit. Application of the FRAX tool will help identify the men at highest risk.

Peter R. Ebeling, M.D.

University of Melbourne  
Parkville, VIC 3052, Australia  
peterre@unimelb.edu.au

1. Kanis JA, Oden A, Johnell O, et al. The use of clinical risk factors enhances the performance of BMD in the prediction of hip and osteoporotic fractures in men and women. *Osteoporos Int* 2007;18:1033-46.
2. Boonen S, Wenderoth D, Schofield PJ, Cahall D, Orwoll ES. Oral risedronate treatment in men with osteoporosis: study design and baseline characteristics. *J Bone Miner Res* 2005;20:Suppl 1:S282. abstract.

## Sublingual Immunotherapy

**TO THE EDITOR:** In his discussion of allergic rhinitis and the clinical use of sublingual immunotherapy, Frew (May 22 issue)<sup>1</sup> reports that the adverse effects of such therapy have been limited mainly to the oral cavity, with only a few cases of anaphylaxis reported. To our knowledge, the studies whose results have been published so far did not look into the incidence of eosinophilic esophagitis with sublingual immunotherapy. Eosinophilic esophagitis is an emerging worldwide disease of unknown cause that mimics gastroesophageal reflux disease and can lead to esophageal narrowing and stricture.<sup>2</sup> The majority of patients with the condition have evidence of food and aeroallergen hypersensitivity. However, only a minority of patients have a history of anaphylaxis, suggesting a dis-

tinct mechanism of IgE-mediated activation of mast cells and basophils.<sup>3</sup> A temporal association between eosinophilic esophagitis and pollen exposure has been described.<sup>4</sup> It is plausible that the repeated delivery of specific allergens through sublingual immunotherapy could lead to delayed cell-mediated responses within the esophagus. We wonder whether an evaluation of the long-term incidence or aggravation of eosinophilic esophagitis with such therapy is warranted.

Arturo J. Bonnin, M.D.

Dawn M. Zacharias, M.D.

Wright State University Boonshoft School of Medicine  
Dayton, OH 45458

1. Frew AJ. Sublingual immunotherapy. *N Engl J Med* 2008; 358:2259-64.