BONE HEALTH

Postmenopausal bone loss places a large disease burden on older women. In this article: latest ACP treatment guidelines, news on fracture risk after stopping hormone therapy, and insights on a popular fracture prediction tool.

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Bone health remains one of the most important health care concerns in the United States today. In 2004, the Surgeon General released a report on bone health and osteoporosis. According to the report's introduction:

> This first-ever Surgeon General's Report on bone health and osteoporosis illustrates the large burden that bone disease places on our Nation and its citizens. Like other chronic diseases that disproportionately affect the elderly, the prevalence of bone disease and fractures is projected to increase markedly as the population ages. If these predictions come true, bone disease and fractures will have a tremendous negative impact on the future well-being of Americans. But as this report makes clear, they need not come true: by working together we can change the picture of aging in America. Osteoporosis and fractures…no longer should be thought of as an inevitable part of growing old. By focusing on prevention and lifestyle changes, including physical activity and nutrition, as well as early diagnosis and appropriate treatment, Americans can avoid much of the damaging impact of bone disease.[1]

Although men also experience osteoporosis as they age, in women the rapid loss of bone at menopause makes their disease burden much greater. As women's health care providers, we stand at the front line for preventing, diagnosing, and treating osteoporosis to reduce the impact of this disease. In this Update I focus on important information that has emerged in the past year.

Guidelines for therapy: How to assess fracture risk and when to treat

American College of Obstetricians and Gynecologists Committee on Practice Bulletins—Gynecology. ACOG Practice Bulletin No. 129: Osteoporosis. Obstet Gynecol. 2012;120(3):718–734.

Qaseem A, Forciea MA, McLean RM, Denberg TD; Clinical Guidelines Committee of the American College of Physicians. Treatment of low bone density or osteoporosis to prevent fractures in men and women: a clinical

IN THIS ARTICLE

ON THE WEB

WATCH: "How do you assess a patient for a bisphosphonate drug holiday?" from Michael McClung, MD, at obgmanagement.com

practice guideline update from the American College of Physicians. Ann Intern Med. 2017;166(11):818–839.

A crucial component for good bone health maintenance and osteoporotic fracture prevention is understanding the current guidelines for therapy. The most recent practice bulletin of the American College of Obstetricians and Gynecologists (ACOG) on osteoporosis was published in 2012. ACOG states that treatment be recommended for women who have a bone mineral density (BMD) T-score of -2.5 or lower.

For women in the low bone mass category (T-score between -1 and -2.5), use of the Fracture Risk Assessment Tool (FRAX) calculator can assist in making an informed treatment decision.[2] Based on the FRAX calculator, women who have a 10-year risk of major osteoporotic fracture of 20% or greater, or a risk of hip fracture of 3% or greater, are candidates for pharmacologic therapy.

Women who have experienced a low-trauma fracture (especially of the vertebra or hip) also are candidates for treatment, even in the absence of osteoporosis on a dual-energy x-ray absorptiometry (DXA) report.

FAST TRACK

The ACP recommends that clinicians treat osteoporotic women with pharmacologic therapy for 5 years

Updated recommendations from the ACP

The 2017 guideline published by the American College of Physicians (ACP), whose target audience is "all clinicians," recommends that, for women who have known osteoporosis, clinicians offer pharmacologic treatment with alendronate, risedronate, zoledronic acid, or denosumab to reduce the risk for hip and vertebral fractures.

In addition, the ACP recommends that clinicians make the decision whether or not to treat osteopenic women 65 years of age or older who are at a high risk for fracture based on a discussion of patient preferences, fracture risk profile, and benefits, harms, and costs of medications. This may seem somewhat contradictory to ACOG's guidance vis-a-vis women younger than 65 years of age.

The ACP further states that given the limited evidence supporting the benefit of treatment, the balance of benefits and harms in treating osteopenic women is most favorable when the risk for fracture is high. Women younger than 65 years with osteopenia and women older than 65 years with mild osteopenia (T-score between -1.0 and -1.5) will benefit less than women who are 65 years of age or older with severe osteopenia (T-score <-2.0).

Risk factors and risk assessment tools

Clinicians can use their own judgment based on risk factors for fracture (lower body weight, smoking, weight loss, family history of fractures, decreased physical activity, alcohol or caffeine use, low calcium and vitamin D intake, corticosteroid use), or they can use a risk assessment tool. Several risk assessment tools, such as the FRAX calculator mentioned earlier, are available to predict fracture risk among untreated people with low bone density. Although the FRAX calculator is widely used, there is no evidence from randomized controlled trials demonstrating a benefit of fracture reduction when FRAX scores are used in treatment decision making.

Duration of therapy. The ACP recommends that clinicians treat osteoporotic women with pharmacologic therapy for 5 years. Bone density monitoring is not recommended during the 5-year treatment period for osteoporosis in women; current evidence does not show any benefit for bone density monitoring during treatment.

Moderate-quality evidence demonstrated that women treated with antiresorptive therapies (including bisphosphonates, raloxifene, and teriparatide) benefited from reduced fractures, even if no increase in BMD occurred or if BMD decreased.

WHAT THIS EVIDENCE MEANS FOR PRACTICE

As before, all women with osteoporosis or a previous low-trauma fracture should be treated. Use of the FRAX calculator should involve clinician judgment, and other risk factors should be taken into account. For most women, treatment should be continued for 5 years. There is no benefit in continued bone mass assessment (DXA testing) while a patient is on pharmacologic therapy.

Another WHI update: No increase in fractures after stopping HT

Watts NB, Cauley JA, Jackson RD, et al; Women's Health Initiative Investigators. No increase in fractures after stopping hormone therapy: results from the Women's Health Initiative. J Clin Endocrinol Metab. 2017;102(1):302–308.

The analysis and reanalysis of the Women's Health Initiative (WHI) trial data seems never-ending, yet the article by Watts and colleagues is important. Although the WHI hormone therapy (HT) trials showed that treatment protects against hip and total fractures, a later observational report suggested loss of benefit and rebound increased risk after HT was discontinued.[3] The purpose of the Watts' study was to examine fractures after stopping HT.

Details of the study

Two placebo-controlled randomized trials served as the study setting. The study included WHI participants (n = 15,187) who continued to take active HT or placebo through the intervention period and who did not take HT in the postintervention period. The trial interventions included conjugated equine estrogen (CEE) plus medroxyprogesterone acetate (MPA) for women with natural menopause and CEE alone for women with prior hysterectomy. The investigators recorded total fractures and hip fractures through 5 years after HT discontinuation.

Findings on fractures. Hip fractures occurred infrequently, with approximately 2.5 per 1,000 person-years. This finding was similar between trials and in former HT users and placebo groups.

No difference was found in total fractures in the CEE plus MPA trial for former HT users compared with former placebo users (28.9 per 1,000 person-years and 29.9 per 1,000 person-years, respectively; hazard ratio [HR], 0.97; 95% confidence interval [CI], 0.87–1.09; $P = .63$). In the CEE-alone trial, however, total fractures were higher in former placebo users (36.9 per 1,000 person-years) compared with the former active-treatment group (31.1 per 1,000 person-years). This finding suggests a residual benefit of CEE in reducing total fractures (HR, 0.85; 95% CI, 0.73–0.98; $P = .03$).

Investigators' takeaway. The authors concluded that, after discontinuing HT, there was no evidence of increased fracture risk (sustained or transient) in former HT users compared with former placebo users. In the CEE-alone trial, there was a residual benefit for total fracture reduction in former HT users compared with placebo users.

WHAT THIS EVIDENCE MEANS FOR PRACTICE

Gynecologists have long believed that on stopping HT, the loss of bone mass will follow at the same rate as it would at natural menopause. These WHI trials demonstrate, however, that through 5 years, women who stopped HT had no increase in hip or total fractures, and hysterectomized women who stopped estrogen therapy actually had fewer fractures than the placebo group. Keep in mind that this large cohort was *not* chosen based on risk of osteoporotic fractures. In fact, baseline bone mass was not even measured in these women, making the results even more "real world."

FAST TRACK

After stopping therapy, CEE-alone users had fewer total fractures compared with placebo users (31.1 vs 36.9 per 1,000 person-years), suggesting a residual benefit of CEE in reducing total fractures

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›› **Update on obstetrics** from Jaimey Pauli, MD, *coming in January*

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A new look at fracture risk assessment scores

Gourlay ML, Overman RA, Fine JP, et al; Women's Health Initiative Investigators. Time to clinically relevant fracture risk scores in postmenopausal women. Am J Med. 2017;130:862.e15–e23.

Jiang X, Gruner M, Trémollieres F, et al. Diagnostic accuracy of FRAX in predicting the 10-year risk of osteoporotic fractures using the USA treatment thresholds: a systematic review and meta-analysis. Bone. 2017;99:20–25.

FAST TRACK

Of 6,096 women who had FRAX scores calculated with bone mineral density testing, estimated unadjusted time to treatment-level FRAX scores was 7.6 years for women aged 65 to 69 and 5.1 years for those aged 75 to 79 at baseline

The FRAX score has become a popular form of triage for women who do not yet meet the bone mass criteria of osteoporosis. Current practice guidelines recommend use of fracture risk scores for screening and pharmacologic therapeutic decision making. Some newer data, however, may give rise to questions about its utility, especially in younger women.

Fracture risk analysis in a large postmenopausal population

Gourlay and colleagues conducted a retrospective competing risk analysis of new occurrence of treatment-level and screening-level fracture risk scores. Study participants were postmenopausal women aged 50 years and older who had not previously received pharmacologic treatment and had not had a first hip or clinical vertebral facture.

Details of the study

In 54,280 postmenopausal women aged 50 to 64 years who did not have a bone mineral density test, the time for 10% to develop a treatment-level FRAX score could not be estimated accurately because the incidence of treatment-level scores was rare.

A total of 6,096 women had FRAX scores calculated *with* bone mineral density testing. In this group, the estimated unadjusted time to treatment-level FRAX scores was 7.6 years (95% CI, 6.6–8.7) for those aged 65 to 69, and 5.1 years (95% CI, 3.5–7.5) for women aged 75 to 79 at baseline.

Of 17,967 women aged 50 to 64 who had a screening-level FRAX at baseline, 100 (0.6%) experienced a hip or clinical vertebral fracture by age 65 years.

Age is key factor. Gourlay and colleagues concluded that postmenopausal women who had subthreshold fracture risk scores at baseline would be unlikely to develop a treatment-level FRAX score between ages 50 and 64. The increased incidence of treatment-level fracture risk scores, osteoporosis, and major osteoporotic fracture after age 65, however, supports more frequent consideration of FRAX assessment and bone mineral density testing.

Meta-analysis of FRAX tool accuracy

In another study, Jiang and colleagues conducted a systematic review and meta-analysis to determine how the FRAX score performed in predicting the 10-year risk of major osteoporotic fractures and hip fractures. The investigators used the US treatment thresholds.

Details of the study

Seven studies (n = 57,027) were analyzed to assess the diagnostic accuracy of FRAX in predicting major osteoporotic fractures; 20% was used as the 10-year fracture risk threshold for intervention. The mean sensitivity and specificity, along with their 95% CIs, were 10.25% (3.76%–25.06%) and 97.02% (91.17%–99.03%), respectively.

For hip fracture prediction, 6 studies (n = 50,944) were analyzed, and 3% was used as the 10-year fracture risk threshold. The mean sensitivity and specificity, along with their 95% CIs, were 45.70% (24.88%–68.13%) and 84.70% (76.41%–90.44%), respectively.

Predictive value of FRAX. The authors

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concluded that, using the 10-year intervention thresholds of 20% for major osteoporotic fracture and 3% for hip fracture, FRAX performed better in identifying individuals who will not have a major osteoporotic fracture or hip fracture within 10 years than in identifying those who will experience a fracture. A substantial number of those who developed fractures, especially major osteoporotic fracture within 10 years of follow up, were missed by the baseline FRAX assessment.

WHAT THIS EVIDENCE MEANS FOR PRACTICE

Increasing age is still arguably among the most important factors for decreasing bone health. Older women are more likely to develop treatment-level FRAX scores more quickly than younger women. In addition, the FRAX tool is better in predicting which women will *not* develop a fracture in the next 10 years than in predicting those who will experience a fracture.

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