JAMA Insights | WOMEN'S HEALTH

Osteoporosis Screening in Younger Postmenopausal Women

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Osteoporotic fractures, especially hip fractures, are associated with mobility limitations, chronic disability, loss of independence, and reduced quality of life.

Several randomized trials have demonstrated the benefit of drug treatment in reducing clinical fractures among postmenopausal women with existing vertebral fractures or bone mineral density (BMD) T-scores of −2.5 or lower and among adults aged 50 years and older with recent hip fracture.

Thus, osteoporosis in the clinical setting should be diagnosed in patients with a history of hip or clinical vertebral fracture not due to excessive trauma, those with existing radiographic vertebral fractures, and those with a BMD T-score of −2.5 or lower at the hip (femoral neck or total hip) or lumbar spine. In the absence of a history of hip or vertebral fracture, osteoporosis screening is aimed at identifying individuals with a BMD T-score of −2.5 or lower because those individuals may be candidates for osteoporosis pharmacotherapy. The BMD T-score quantifies the difference (expressed in standard deviations) between a patient's BMD and the average BMD of young adult white women (reference group).

The prevalence of primary osteoporosis (osteoporosis not due to secondary causes, eg, malabsorption syndrome) increases with age and differs by sex and race/ethnicity. While professional societies and the US Preventive Services Task Force (USPSTF)[1] universally recommend routine osteoporosis screening with BMD testing among women aged 65 years and older, there is controversy regarding osteoporosis screening in postmenopausal women younger than 65 years.

The absolute fracture risk for any given BMD is much lower in younger postmenopausal women than in older women. According to a 2001 report, the estimated 5-year probability of clinical spine fracture among postmenopausal women is 0.3% for women aged 50 to 54 years at baseline, 0.5% for women aged 55 to 59 years, and 1.0% for women aged 60 to 64 years.[2] The estimated 5-year probability of hip fracture is 0.0% for women aged 50 to 54 years, 0.2% for women aged 55 to 59 years, and 0.2% for women aged 60 to 64 years.[2] In addition, in part because of the duration-dependence of atypical femoral fractures associated with potent antiresorptive osteoporosis medication, the use of osteoporosis drug treatment in younger women may leave them with fewer options for pharmacologic therapy in their 70s, when their risk of fracture, especially hip fracture, begins to accelerate.

Some professional organizations recommend osteoporosis screening in younger postmenopausal with a clinical risk factor for fracture. However, there is no consensus regarding the specific risk factors that should be considered in this decision. In contrast, the USPSTF in 2018 recommended osteoporosis screening in younger postmenopausal women (ie, <65 years) identified to be at increased risk of osteoporosis (low body weight, parental history of hip fracture, smoking) using a formal risk assessment tool.[1] Of the 5 tools suggested for use by the USPSTF, 4 tools (the Osteoporosis Self-Assessment Tool [OST], the Osteoporosis Risk Assessment Instrument [ORAI], the Osteoporosis Index of Risk [OSIRIS], and the Simple Calculated Osteoporosis Risk Estimation [SCORE]) were specifically designed to identify individuals with a BMD T-score of −2.5 or lower. The other tool (FRAX, the Fracture Risk Assessment Tool), a web-based calculator, was designed to estimate 10-year probabilities of hip and major osteoporotic fracture using clinical risk factors with or without femoral neck BMD. For each tool, the USPSTF recommended a specific threshold indicating a younger postmenopausal woman at increased risk of osteoporosis. For OST, the simplest calculator that is based on age and weight alone, the threshold is a score less than 2. For FRAX, the most complex tool, the USPSTF-recommended threshold is a 10-year probability of major osteoporotic fracture (calculated without BMD) of 8.4% or higher, because 8.4% is the estimated 10-year probability of major osteoporotic fracture in a 65-year-old white woman of average height and weight without additional risk factors (**Figure**).

Comparisons of the OST threshold vs FRAX threshold recommended by USPSTF among postmenopausal women aged younger than 65 years report higher combined sensitivity and specificity and better discrimination with the OST threshold. For example, for identifying femoral neck BMD T-score of −2.5 or lower, the OST threshold had a sensitivity of 79%, a specificity of 70%, and an area under the receiver operating characteristic curve (AUC) of 0.75. In contrast, the FRAX threshold had sensitivity of approximately 30%, specificity of 86%, and AUC of 0.60.[3,4] Varying the cutoffs of the tools did not improve AUC values.[3] The FRAX threshold is only slightly better than chance alone (AUC of 0.50), whereas the OST threshold has good performance (AUC >0.70). Considering the tradeoff between sensitivity and specificity, and the much higher sensitivity of OST compared with FRAX at recommended thresholds, OST appears to be preferable to FRAX for identifying younger postmenopausal women with a BMD T-score of −2.5 or lower. On balance, although a single tool is unlikely to be optimal for every setting, OST seems to be the tool better suited for screening, on the basis of its higher sensitivity (and its clinical tractability).

There are few data comparing the performance of the tools in identifying younger postmenopausal women who actually go on to experience incident fractures. One study involving 62 492 postmenopausal women compared the performance of OST vs FRAX thresholds in identifying women aged 50 to 64 years who experienced major osteoporotic fracture during 10 years of follow-up. Annualized rates of major osteoporotic fracture were 0.53% (95% CI, 0.51%-0.54%) in women with predicted risk below the FRAX threshold and 0.91% (95% CI, 0.86%-0.95%) in women at or above the FRAX threshold. The OST threshold had a sensitivity of 40%, a specificity of 66%, and an AUC of 0.56, whereas the FRAX threshold had a sensitivity of 25%, a specificity of 83%, and an AUC of 0.56.[5] The low sensitivities indicate that neither OST nor FRAX identifies the majority of women who will experience major osteoporotic fracture . Varying the thresholds for the tools did not improve the AUC values, which remained near 0.50, indicating poor discrimination.[5] For example, a FRAX cutoff of at least 3.75 (ie, 10-year FRAX-predicted risk of major osteoporotic fracture of ≥3.75%) identified 90% of postmenopausal women aged 50 to 64 years with incident major osteoporotic fracture during the subsequent 10 years. However, the specificity of that approach was only 16%.[5] Therefore, this limited available evidence suggests that neither OST nor

Figure. Selecting Candidates for Bone Density Testing in Younger Postmenopausal Women at Increased Risk for Osteoporosis

Tools for the assessment of bone mineral density and threshold scores to indicate bone density testing

Osteoporosis Self-Assessment Tool (OST)

Risk factors	Scoring
• Weight, kg	(kg − y) × 0.2
• Age, y	

Threshold score <2

Osteoporosis Index of Risk (OSIRIS)

Risk factors	Scoring
• Age, y	y × −0.2
• Weight, kg	kg × 0.2
• Current estrogen use	2
• Prior low-impact fracture	−2

Threshold score <1

Osteoporosis Risk Assessment Instrument (ORAI)

Risk factors	Scoring
• Age, y	
55-64	5
45-54	0
• Weight, kg	
<60	9
60-69	3
≥70	0
• No current estrogen use	2

Threshold score ≥9

Simple Calculated Osteoporosis Risk Estimation (SCORE)

Risk factors	Scoring
• Age, y	3 × first digit of age
• Weight, lb	−1 × (lb ÷ 10)[a]
• No estrogen use	1
• Nonblack race	5
• Rheumatoid arthritis	4
• Prior fracture after age 45 (nontraumatic rib, wrist, or hip)	4 per each type (max 12)

Threshold score ≥6

Fracture Risk Assessment Tool (FRAX)

Risk factors	
• Age, y	• Height, cm
• Sex	• Current smoking
• Weight, kg	• Prior fracture
• Alcohol consumption ≥3 U/d	
• Rheumatoid arthritis	
• Parental hip fracture	
• Corticosteroid use	
• Secondary osteoporosis	

Scoring by proprietary formula

Predicted risk of MOF ≥8.4%

Clinical risk factors associated with osteoporosis and related fractures include low body weight, parental history of hip fracture, and smoking. MOF indicates major osteoporotic fracture.

[a] The results should be truncated to the integer.

FRAX performs adequately in identifying younger postmenopausal women who will experience incident fractures.

Future Directions

The optimal osteoporosis screening strategy in younger postmenopausal women remains unknown. No randomized clinical trials have tested whether the use of formal risk assessment tools to select candidates for BMD testing decreases fracture incidence in this patient population.

The USPSTF highlights that a high priority for future research is determining whether clinical risk assessment tools alone (without BMD information) can identify patients at risk for fracture in this age group. The development of tools to predict fracture is challenging in part due to the heterogeneity of fracture circumstances in this patient population (some being related to higher-impact activity and risk-taking behavior while others are more typical low-trauma fractures characteristic of older women).

Research evaluating best strategies for pharmacologic treatment in younger postmenopausal women with osteoporosis is also needed because long-term (≥10 years) treatment may not be the optimal strategy given the reported duration-dependent risk of atypical femoral fracture associated with use of potent antiresorptive therapy.

The Bottom Line

"Need a baseline" is not a strong rationale for ordering BMD testing in younger postmenopausal women. The absolute risk of fracture is low in postmenopausal women younger than 65 years. To select postmenopausal women younger than 65 years for BMD testing, the USPSTF strategy is preferred: screening women younger than 65 years at increased risk of osteoporosis (eg, low body weight, parental history of hip fracture, smoking) using a formal risk assessment tool to identify candidates for bone density testing. Of the formal risk calculators, the OST tool (threshold score <2) is recommended because it has the simplest formula (based on age and weight) and performs as well as or better than the more complex tools (FRAX, ORAI, OSIRIS, SCORE) for identifying younger postmenopausal women with a BMD T-score of −2.5 or lower. Prior to ordering BMD testing in this patient population, clinicians need to carefully counsel women about the benefits and risks of osteoporosis drug treatment at this stage of life.

ARTICLE INFORMATION

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Published Online: January 9, 2020. doi:10.1001/jama.2019.18343

Conflict of Interest Disclosures: Dr Ensrud reported receiving grants from Merck & Co outside the submitted work. No other disclosures were reported.

Submissions: The Women's Health editors welcome proposals for features in the section. Submit yours to ccrandall@mednet.ucla.edu or edward.livingston@jamanetwork.org.

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