

Screening for Osteoporosis in Postmenopausal Women: Recommendations and Rationale: U.S. Preventive Services Task Force

United States Preventive Services Task Force

Citation

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Abstract

Figure 3



Agency for Healthcare Research and Quality

Figure 2



US Department of Health and Human Services

SUMMARY OF RECOMMENDATIONS

The U.S. Preventive Services Task Force (USPSTF)

recommends that women aged 65 and older be screened routinely for osteoporosis. The USPSTF recommends that routine screening begin at age 60 for women at increased risk for osteoporotic fractures (see "Clinical Considerations" for discussion of women at increased risk). B recommendation.

The USPSTF found good evidence that the risk for osteoporosis and fracture increases with age and other factors, that bone density measurements accurately predict the risk for fractures in the short-term, and that treating asymptomatic women with osteoporosis reduces their risk for fracture. The USPSTF concludes that the benefits of screening and treatment are of at least moderate magnitude for women at increased risk by virtue of age or presence of other risk factors.

The USPSTF makes no recommendation for or against routine osteoporosis screening in postmenopausal women who are younger than 60 or in women aged 60-64 who are not at increased risk for osteoporotic fractures. C recommendation.

The USPSTF found fair evidence that screening women at lower risk for osteoporosis or fracture can identify additional women who may be eligible for treatment for osteoporosis, but it would prevent a small number of fractures. The USPSTF concludes that the balance of benefits and harms of screening and treatment is too close to make a general recommendation for this age group.

CLINICAL CONSIDERATIONS

- Modeling analysis suggests that the absolute benefits of screening for osteoporosis among women aged 60-64 who are at increased risk for

osteoporosis and fracture are comparable to those of routine screening in older women. The exact risk factors that should trigger screening in this age group are difficult to specify based on evidence. Lower body weight (weight 70 kg) is the single best predictor of low bone mineral density. 4,5 Low weight and no current use of estrogen therapy are incorporated with age into the 3-item Osteoporosis Risk Assessment Instrument (ORAI). 4,5 There is less evidence to support the use of other individual risk factors (for example, smoking, weight loss, family history, decreased physical activity, alcohol or caffeine use, or low calcium and vitamin D intake) as a basis for identifying high-risk women younger than 65. At any given age, African American women on average have higher bone mineral density (BMD) than white women and are thus less likely to benefit from screening. Additional characteristics of screening tools are discussed in the “Accuracy and Reliability of Screening Tests” section below.

- Among different bone measurement tests performed at various anatomical sites, bone density measured at the femoral neck by dual-energy x-ray absorptiometry (DXA) is the best predictor of hip fracture and is comparable to forearm measurements for predicting fractures at other sites. Other technologies for measuring peripheral sites include quantitative ultrasonography (QUS), radiographic absorptiometry, single energy x-ray absorptiometry, peripheral dual-energy x-ray absorptiometry, and peripheral quantitative computed tomography. Recent data suggest that peripheral bone density testing in the primary care setting can also identify postmenopausal women who have a higher risk for fracture over the short term (1 year). Further research is needed to determine the accuracy of peripheral bone density testing in comparison with dual-energy x-ray absorptiometry (DXA). The likelihood of being diagnosed with osteoporosis varies greatly depending on the site and type of bone measurement test, the number of sites tested, the brand of densitometer used, and the relevance of the reference range.
- Estimates of the benefits of detecting and treating

osteoporosis are based largely on studies of bisphosphonates. Some women, however, may prefer other treatment options (for example, hormone replacement therapy, selective estrogen receptor modulators, or calcitonin) based on personal preferences or risk factors. Clinicians should review with patients the relative benefits and harms of available treatment options, and uncertainties about their efficacy and safety, to facilitate an informed choice.

- No studies have evaluated the optimal intervals for repeated screening. Because of limitations in the precision of testing, a minimum of 2 years may be needed to reliably measure a change in bone mineral density; however, longer intervals may be adequate for repeated screening to identify new cases of osteoporosis. Yield of repeated screening will be higher in older women, those with lower BMD at baseline, and those with other risk factors for fracture.
- There are no data to determine the appropriate age to stop screening and few data on osteoporosis treatment in women older than 85. Patients who receive a diagnosis of osteoporosis fall outside the context of screening but may require additional testing for diagnostic purposes or to monitor response to treatment.

SCIENTIFIC EVIDENCE

EPIDEMIOLOGY AND CLINICAL CONSEQUENCES

One-half of all postmenopausal women will have an osteoporosis-related fracture during their lives, including 25% who will develop a vertebral deformity⁶ and 15% who will suffer a hip fracture.⁷ Risk for fracture increases steadily as bone density declines, with no threshold. The commonly used definition of osteoporosis, derived from the World Health Organization (WHO) recommendations for epidemiologic studies, defines a BMD more than 2.5 standard deviations (SD) below the mean for a young healthy adult woman as osteoporosis, and a BMD between 1 and 2.5 SD below the mean as osteopenia. Based on the WHO criteria and DXA measurements at the femoral neck, population-based studies estimate that 41% of white women older than 50 have osteopenia.⁸ When bone density is measured at the hip, spine, and wrist, 15% of white women

aged 50-59 and 70% of white women older than 80 have osteoporosis by WHO criteria at at least one site.⁹

The prevalence of osteoporosis in Mexican American women is similar to the prevalence in white women. While rates of osteoporosis in African American women are approximately one-half those of the other groups, they are still substantial (8% among women older than 50). Including all races, an estimated 14 million women older than 50 have osteopenia, and over 5 million have osteoporosis.¹⁰ The actuarial risk of a 65-year-old white woman sustaining a fracture by age 90 is 16% for the hip, 9% for distal forearm, and 5% for proximal humerus.⁹ Sixteen percent of postmenopausal women have osteoporosis of the lumbar spine.¹¹

ACCURACY AND RELIABILITY OF SCREENING TESTS

The USPSTF examined 2 components of screening: the accuracy of risk factors or risk assessment instruments for identifying women at risk for osteoporosis or fracture; and the accuracy of different bone density measurement techniques for identifying women at risk for fracture who can benefit from osteoporosis treatment.

Predicting Risk for Osteoporosis or Fracture

The USPSTF evaluated both individual risk factors and prescreening assessment tools that incorporate two or more of the risk factors. Risk for osteoporosis increases steadily and substantially with age. Relative to women aged 50-54, the odds of having osteoporosis were 5.9-fold higher in women aged 65-69 and 14.3-fold higher in women aged 75-79, in a study of over 200,000 postmenopausal women.¹² Low body weight or body-mass index (BMI) and not using estrogen replacement were also consistently associated with osteoporosis but to a lesser degree than age. Other risk factors for fracture or low bone density found in some, but not all, studies include white or Asian ethnicity, history of fracture, family history of osteoporotic fracture, history of falls, low levels of physical activity, smoking, excessive alcohol or caffeine use, low calcium or vitamin D intake, and the use of various medications.

Specific instruments to assess risk for low bone density or fractures generally have moderate-to-high sensitivity and low specificity. The best validated instruments include the 3-item ORAI and the 6-item Simple Calculated Osteoporosis Risk Estimation tool (SCORE). The ORAI uses age, weight,

and current use of hormone replacement therapy to identify women at risk for osteoporosis and has a sensitivity of 94% and specificity of 41%.⁴ The SCORE has a sensitivity of 91% and specificity of 40% in one validation population (n = 259), but it has much lower specificity in an older population.¹¹

Among 8 studies of prediction instruments for fracture risk, most had only modest sensitivity and specificity. The best performing model for hip fracture outcomes included age, gender, height, use of a walking aid, current smoking, and weight and had a sensitivity of 70% with specificity of 84%.¹³

Measurements of Bone Density

To date, bone density measured at the femoral neck by DXA is the best predictor of hip fracture and is comparable to forearm measurements for predicting fractures at other sites. Recent prospective studies have evaluated QUS measurements at the heel.^{14, 15} While QUS measurements are not highly correlated with DXA measurements, a result in the osteoporotic range on either test is associated with an increased short-term probability of hip fracture. Several other radiologic methods that measure bone density at peripheral sites² (including sites in the hand, heel, wrist, and forearm) include single photon absorptiometry, quantitative computed tomography, single-energy x-ray absorptiometry, and peripheral quantitative computed tomography. In a study of over 200,000 women in a primary care setting, women diagnosed with osteoporosis by peripheral bone density measurements were 4 times more likely to have fractures than women with normal bone density over the subsequent year. The likelihood of being diagnosed with osteoporosis varies greatly depending on the site and type of bone measurement test, the number of sites tested, the brand of densitometer, and the relevance of the reference range.

EFFECTIVENESS OF EARLY TREATMENT

No controlled studies have evaluated the effect of screening on fractures or fracture-related morbidity. The Task Force reviewed the evidence to determine whether treatment for osteoporosis or low bone density in asymptomatic patients reduced fractures.

Available trials that reported fracture outcomes have examined the efficacy of bisphosphonates (alendronate and risendronate), estrogen, and selective estrogen receptor modulators (raloxifene) and calcitonin. A meta-analysis¹⁶ of

11 randomized trials¹⁷⁻²⁷ involving a total of 12,855 women, found that alendronate significantly reduced vertebral fractures (RR, 0.52; 95% CI, 0.43-0.65), forearm fractures (RR, 0.48; 0.29-0.78), hip fractures (RR, 0.63; 0.43-0.92), and other nonvertebral fractures (RR, 0.51; 0.38-0.69). There were non-significant trends toward reduction in hip fractures. No randomized trial of treatment for osteoporosis has demonstrated an impact on mortality. One trial in women aged 70-79 with very low bone density (T-score less than -3) reported that risendronate reduced the risk for hip fracture (RR, 0.60; 95% CI, 0.40-0.90).²⁸

There are no direct comparisons of alendronate and estrogen or raloxifene that report fracture outcomes. Estrogen, either alone or with progestin, consistently improves bone density in randomized trials. The effects of estrogen and the selective estrogen receptor modulators on fractures are reviewed in more detail in a separate report.¹³ Only a few small randomized clinical trials of estrogen indicate mixed results for fracture outcomes, but these studies are methodologically limited. Observational studies report a 25% to 30% reduction in the risk for hip fracture with estrogen use. A good-quality study of raloxifene reported a reduced risk for vertebral fractures (RR, 0.59; 95% CI, 0.50-0.70).²⁹

The benefits of treating osteoporosis are larger in women at higher risk for fracture than in women at lower risk. The Fracture Intervention Trial (FIT) was conducted with 2 different groups of participants: 2,027 high-risk women who had T-scores of -1.6 or lower and pre-existing vertebral fractures, and 4,432 women with comparable T-scores but no pre-existing vertebral fracture. Over 3 years of treatment in high-risk women, alendronate reduced the risk for hip fracture (1.1% vs. 2.2% in the placebo group; relative hazard [RH], 0.49 [0.23-.099]) and the risk for any clinical fracture (18.2% vs. 13.6%; RH 0.72 [0.58-0.90]). Among women with no pre-existing fracture, only the subgroup of patients who had a T-score less than -2.5 had a significant reduction in all clinical fractures from treatment, from 19.6% to 13.1% (RR, 0.64; 0.50-0.82). Alendronate had no effect on fractures among lower risk women who had T-scores between -1.6 and -2.5. These results suggest that treatment will produce larger benefits in women with more risk factors for fracture, such as those who are older, have very low bone density, or have pre-existing vertebral fractures. FIT, as well as other therapy trials, enrolled highly selected patients thus limiting the generalizability of their results to asymptomatic

women detected in a typical primary care setting.

There is little evidence regarding which patients are likely to benefit from screening and treatment. It is not known whether women who have a similar overall risk for fracture, but different bone densities, will benefit similarly from treatment. This uncertainty is clinically important because the lack of accepted criteria for initiating treatment remains a problem.

To estimate the benefits of routine screening for women in different age groups, the USPSTF used estimates from recent studies to project the number of fractures that would be prevented over 5 years from screening and treatment of a hypothetical cohort of 10,000 postmenopausal women.² For women aged 55-59, more than 4,000 would need to be screened to prevent 1 hip fracture and more than 1,300 to prevent 1 vertebral fracture. For women older than 60, the number needed to screen to prevent 1 hip fracture is 1,856 for women aged 60-64, 731 for women aged 65-69, and 143 for women aged 75-79. The benefits of screening improve substantially in older women because osteoporosis is both more prevalent and more likely to lead to a fracture in older women.

In all age groups, the number needed to screen to prevent fractures is lower in women with important risk factors than it is in women who do not have risk factors. For women aged 60-64 who have a risk factor that increases the risk of osteoporosis by 100% and fracture by 70%, the number needed to screen is 1,092 and the number need to treat is 72 to prevent 1 hip fracture. These numbers are comparable to those of women aged 65-69 without risk factors.² These estimates rely on many assumptions that may not apply for specific populations.

POTENTIAL ADVERSE EFFECTS OF SCREENING AND TREATMENT

There are several potential harms of screening, although the empirical data for them are few. Women who undergo screening with bone density tests are more likely to begin hormone replacement therapy than women who do not. However, women who were diagnosed with osteoporosis after screening reported increased fears and anxiety in one study. Other potential harms may arise from inaccuracies and misinterpretations of bone density tests. Clinicians may have difficulty in using test results to provide accurate information to the patients because techniques used to measure bone density vary, test results are reported as T-

scores, and information on how to integrate bone density results with other clinical predictors has not been clearly defined.²

In the alendronate treatment trials, gastrointestinal side effects occurred in about 25% of patients taking alendronate, but this was usually not higher (or only slightly higher) than the rate for placebo. Higher rates were observed among Medicare enrollees taking alendronate. In the FIT-II trial, the rates of ulcer disease were higher in the alendronate treatment group, with 2.2 percent developing ulcer disease, as opposed to 1.2 percent in the placebo group ($P < 0.05$).³⁰ The long-term adverse effects of alendronate are unknown. Harms of hormone replacement therapy include venous thromboembolic events, endometrial cancer, and cholecystitis, all with relative risks of approximately 2.0.¹² Both raloxifene and tamoxifen are associated with thromboembolic events, leg cramps, and hot flashes.²

RECOMMENDATIONS OF OTHERS

In 1998, the National Osteoporosis Foundation, in collaboration with other professional organizations, issued screening guidelines recommending bone density testing for all women aged 65 or older and younger postmenopausal women who have had a fracture or who have one or more risk factors for osteoporosis.³¹ Collaborating groups included the American Academy of Orthopaedic Surgeons, the American College of Obstetricians and Gynecologists, the American Geriatrics Society, the American College of Radiology, the American College of Rheumatology, the American Academy of Physical Medicine and Rehabilitation, the American Association of Clinical Endocrinologists, the Endocrine Society, and the American Society of Bone and Mineral Research. The American Association of Clinical Endocrinologists released revised guidelines in 2001.³² A 2000 Consensus Development Conference sponsored by the U.S. National Institutes of Health concluded that the value of universal osteoporosis screening was not yet established.³³ The conference panel recommended an individualized approach to screening, noting that bone density measurement is appropriate when it will aid the patient's decision to institute treatment. The Canadian Task Force on Preventive Health Care is currently revising its recommendations on screening for osteoporosis.

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APPENDIX A

U.S. PREVENTIVE SERVICES TASK FORCE RECOMMENDATIONS AND RATINGS

The Task Force grades its recommendations according to one of 5 classifications (A, B, C, D, I) reflecting the strength of evidence and magnitude of net benefit (benefits minus harms):

A. The USPSTF strongly recommends that clinicians routinely provide [the service] to eligible patients. The USPSTF found good evidence that [the service] improves important health outcomes and concludes that benefits substantially outweigh harms.

B. The USPSTF recommends that clinicians routinely provide [the service] to eligible patients. The USPSTF found at least fair evidence that [the service] improves important health outcomes and concludes that benefits outweigh harms.

C. The USPSTF makes no recommendation for or against routine provision of [the service]. The USPSTF found at least fair evidence that [the service] can improve health outcomes but concludes that the balance of benefits and harms is too close to justify a general recommendation.

D. The USPSTF recommends against routinely providing [the service] to asymptomatic patients. The USPSTF found at least fair evidence that [the service] is ineffective or that harms outweigh benefits.

I. The USPSTF concludes that the evidence is insufficient to recommend for or against routinely providing [the service]. Evidence that the [service] is effective is lacking, of poor quality, or conflicting and the balance of benefits and harms cannot be determined.

APPENDIX B

U.S. PREVENTIVE SERVICES TASK FORCE STRENGTH OF OVERALL EVIDENCE

The USPSTF grades the quality of the overall evidence for a service on a 3-point scale (good, fair, poor):

Good: Evidence includes consistent results from well-designed, well-conducted studies in representative populations that directly assess effects on health outcomes.

Fair: Evidence is sufficient to determine effects on health outcomes, but the strength of the evidence is limited by the

number, quality, or consistency of the individual studies, generalizability to routine practice, or indirect nature of the evidence on health outcomes.

Poor: Evidence is insufficient to assess the effects on health outcomes because of limited number or power of studies, important flaws in their design or conduct, gaps in the chain of evidence, or lack of information on important health outcomes.

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This statement summarizes the current U.S. Preventive Services Task Force (USPSTF) recommendations on screening for osteoporosis and the supporting scientific evidence, and it updates the 1996 recommendations contained in the Guide to Clinical Preventive Services, second edition.¹ Explanations of the ratings and of the strength of overall evidence are given in Appendix A and Appendix B, respectively. The complete information on which this statement is based, including evidence tables and references, is available in the accompanying article, "Screening for osteoporosis: a review of the evidence for the U.S. Preventive Services Task Force"² and in the Systematic Evidence Review³ on this topic, which can be obtained through the USPSTF Web site (<http://www.preventiveservices.ahrq.gov>) and in print through the AHRQ Publications Clearinghouse (call 1-800-358-9295 or e-mail ahrqpubs@ahrq.gov).

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