

HERC Coverage Guidance – Osteoporosis Screening And Monitoring By Dual-Energy X-Ray Absorptiometry (DXA) Disposition of Public Comments

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| <p>E. Michael Lewiecki, MD, FACP, FACE Osteoporosis Director, New Mexico Clinical Research & Osteoporosis Center, Inc., Albuquerque, NM</p> | 1 | <p>Background. Osteoporosis, defined as low bone strength that increases the risk of fractures (1), is a common skeletal disorder that has been identified by the US Surgeon General as a major public health concern (2). About one of every two women and one of every five men will have an osteoporotic fracture in their lifetimes. Osteoporotic fractures are associated with an increase in morbidity and mortality, as well as high healthcare expenses (2). We are fortunately able to easily and inexpensively measure bone mineral density (BMD) by dual-energy X-ray absorptiometry (DXA) (3), assess fracture risk (4), and treat with pharmacological agents to reduce fracture risk (5). However, osteoporosis continues to be underdiagnosed (6) and undertreated (7), with those for whom treatment is started commonly failing to take medication correctly or long enough to achieve the expected benefit (8). This “treatment gap,” the difference between the number of patients who could benefit from treatment and those who actually receive it (9), has created the need for better strategies to reduce the burden of osteoporotic fractures.</p> | Thank you for this background information. |
| <p><i>HERC-appointed Expert</i></p> | 2 | <p>Clinical applications of DXA. DXA is used to measure BMD, predict fracture risk, and monitor the skeletal effects of osteoporosis treatment (10). The National Osteoporosis Foundation (NOF) has developed evidence-based clinical practice guidelines, endorsed by numerous profession societies and updated in 2013, that provide clinicians with indications for BMD testing, treatment of osteoporosis, and monitoring treatment (11). The NOF guidelines state that BMD testing is indicated in the following individuals:</p> <ul style="list-style-type: none"> • Women age 65 and older and men age 70 and older, regardless of clinical risk factors • Younger postmenopausal women, women in the menopausal transition and men age 50 to 69 with clinical risk factors for fracture • Adults who have a fracture after age 50 • Adults with a condition (e.g., rheumatoid arthritis) or taking a medication (e.g., glucocorticoids in a daily dose \geq 5 mg prednisone or equivalent for \geq three months) associated with low bone mass or bone loss | HTAS is aware of the NOF guideline. Methodology for production of the guideline is not described. Funding of the NOF includes a substantial number of industry donors, including Pfizer, Medtronic, Novartis and 15 others. |
| | 3 | <p>The NOF guidelines also describe the use of DXA to monitor osteoporosis therapy, as follows:</p> <ul style="list-style-type: none"> • Serial central DXA testing is an important component of osteoporosis management. • Measurements for monitoring patients should be performed in accordance with medical necessity, expected response and in consideration of local regulatory requirements. NOF recommends that repeat BMD assessments generally agree with Medicare guidelines of every two years, but recognizes that testing more frequently may be warranted in certain clinical situations. | See comment #2. There is no discussion in the NOF guideline about test characteristics (i.e., precision) of DXA; retesting too soon may result in the margin of error of the test being larger than the actual change in the value of the bone density. USPSTF recommendation states: “Because of limitations in the precision of testing, a minimum of 2 years may be needed to reliably measure a change in BMD; |

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| | | Clinical situations for which testing more frequently (e.g., one year interval) is helpful includes patients started on treatment or changing treatment in order to evaluate for treatment effect, and patients on glucocorticoid therapy who are at risk for rapid bone loss. | however, longer intervals may be necessary to improve fracture risk prediction.” Current coverage recommendations allow for more frequent testing in patients for whom there has been a significant change in risk factors other than medication therapy. |
| | 4 | Although concerns have been raised that some screening prevention programs for other chronic diseases do not result in healthcare savings (12), this is not the case for BMD testing in appropriately selected patients. The experience of healthcare systems suggests that increases in BMD testing reduce fracture rates and save money. A 5-year observational study evaluated the clinical and fiscal outcomes of the Geisinger Health System Osteoporosis Disease Management Program from 1996 to 2000 (13). It was found that implementation of osteoporosis guidelines that included increases in BMD testing and treatment was associated with a significant decrease in the age-adjusted incidence of hip fractures and an estimated \$7.8 million reduction in healthcare costs during this 5-year period. | This observational study projected cost savings of this screening program in women over 65, but projected additional expense in the population between 55 and 65. Guidance document recommends screening on all women 65 and over. |
| | 5 | At Kaiser Southern California, an osteoporosis disease management program (“Healthy Bones Program”) was fully implemented in 2002, with a goal of reducing hip fractures by increasing BMD testing rates and treatment in patients at high risk of hip fracture (14;15). It was estimated that in 2006, 935 hip fractures, with an average cost of \$33,000 each, were prevented, resulting in savings of over \$30.8 million for Kaiser (16). Multiple osteoporosis screening strategies have been found to be clinically effective and cost-effective as well (17-19). | Ref #14 not available through OHSU library. Ref #15 is a clinical summary article that includes a brief description of Ref #16, which is a prospective observational study of the “Healthy Bones” program. This included screening of all women over 65, men over 70, patients with history of hip or fragility fracture or on steroids. Ref #17 is a CEA of a variety of different screening strategies. While they report the best strategy with ICER < \$50,000 was initiation of screening at age 55 with DXA and rescreening every 5 years, they note that several strategies using SCORE (a screening tool similar to FRAX) for prescreening were more cost effective, with ICERs < \$30,000. Ref #18 is a position statement of the American College of Preventive Medicine, which states: “All adult patients age ≥ 50 years should be evaluated for risk factors for osteoporosis. Screening with BMD testing for osteoporosis is recommended in women aged 65 years and in men aged 70 years. Younger postmenopausal women and men aged 50–69 years should undergo screening if they have at least one major or two minor risk factors for osteoporosis.” Ref #19 is also a CEA |

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| | | | that concludes “bone densitometry of post-menopausal women who have not had a prior fracture is reasonable from 65-70 years of age, and is perhaps reasonable for men without a prior fracture after the age of 80 years depending on drug costs, the direct medical costs of fractures, fracture disutility, underlying fracture rates in the population and the societal willingness to pay for health benefits.” |
| | 6 | Comments on HERC coverage guidance. Three sources of medical evidence were used in the development of the coverage guidance: 1. USPSTF recommendations for screening for osteoporosis (20;21); 2. a posthoc subgroup analysis of a single observational study in postmenopausal women (22); and the NICE guidelines from the UK (23). There are serious concerns with each of these that limit their applicability in setting rules for DXA coverage in the US. | HTAS acknowledges that these are the source documents, but disagrees that there are serious concerns regarding their use. |
| | 7 | USPSTF recommendations- The USPSTF recommended screening for osteoporosis “in women aged 65 years or older and in younger women whose fracture risk is equal to or greater than that of a 65-year-old white woman who has no additional risk factors.” This was taken almost verbatim for inclusion in the HERC Guidance. However, the proposal very difficult to implement in clinical practice, as it would involve using FRAX without the benefit of BMD, which is not as good a predictor of fracture risk as FRAX with BMD, and assumes that physicians have the time and knowledge to use FRAX regularly and correctly. A 65 year-old Caucasian woman of average height and weight with no risk factors has a FRAX 10-year probability of major osteoporotic fracture of 9.4% and a 10-year probability of hip fracture of 1.4%. If she has low body weight, the numbers are 11% and 3.0%, respectively. If she is Hispanic, it is 6.0% and 1.7%, respectively. If she is Asian, it is 5.9% and 1.7%, respectively. If she is Black, it is 4.7% and 1.3%, respectively. If another fracture risk calculator, such as Garvan, is used for a 65-year old Caucasian woman with no risk factors, there is a 1.2% 5-year risk of hip fracture, a 2.4% 10-year risk of hip fracture, a 6.7% 5-year risk of any fragility fracture, and a 13.9% 10-year risk of any fragility fracture. There are other calculators as well that would generate different numbers. It is simply not feasible in a busy medical practice for any physician to sort through all of this and not possible for a regulatory agency to monitor for compliance. | The USPSTF selected the FRAX tool because “this tool relies on easily obtainable clinical information, such as age, body mass index (BMI), parental fracture history, and tobacco and alcohol use; its development was supported by a broad international collaboration and extensively validated in 2 large U.S. cohorts; and it is freely accessible to clinicians and the public.” HTAS does not agree that it is not feasible for a physician to utilize this tool and believes that there are many who do. Compliance is an issue of implementation and does not impact the recommendations. |
| | 8 | The USPSTF addressed only screening DXA in women; they do not provide guidance on the use of DXA other than screening (e.g., monitoring) or DXA in men. It should be noted that | HTAS is aware that the USPSTF does not address the use of DXA in monitoring, and therefore includes the Gourlay |

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| | | men age 70 and older are at high risk for fracture, and the consequences of fractures in men (morbidity and mortality) are more grave than in women. The adoption of the USPSTF recommendation would serve to reduce the use of DXA in evaluating patients (especially postmenopausal women under age 65 and men) for fracture risk, when the current problem is quite the opposite- too few patients are being screened for osteoporosis. | study in the guidance document to address this void. The USPSTF <u>does</u> address the use of DXA in men, stating that the evidence is insufficient to recommend for or against screening. . |
| | 9 | Gourlay et al study- This analysis of a subset of subjects in the Study of Osteoporotic Fractures (SOF) concluded quite reasonably that older women with very good BMD were unlikely to develop osteoporosis for many years, if ever. However, it was widely misinterpreted in the media, and by some healthcare providers, to mean that DXA is an expensive overused technology that was increasing medical expenses with little benefit. There was a firestorm of protest from many physicians and professional societies to set the story straight, including two where I was an author (24;25). Gourlay et al correctly identified limitations of the study that preclude its applicability to a wider patient population. The study cohort was restricted to pre-selected women ≥ 67 years of age and did not include men or younger postmenopausal women. It is particularly important to note that women in their early postmenopausal years are likely to experience accelerated bone loss that may require short testing intervals (e.g., 1-2 years) to assess. Also excluded from the trial were nearly 50% of the SOF study participants who had a previous diagnosis of osteoporosis (based on a prior hip or clinical vertebral fracture or densitometric evidence of osteoporosis) or who were already on treatment for osteoporosis. | HTAS is aware of the limitations of the Gourlay study. However, no other evidence has been identified or provided that provides evidence supporting a different testing interval. The cited reference #24 is an editorial that is verbatim to the comment provided here. Reference #25 is a letter to the editor. The author's (Gourlay's) response is as follows: "We strongly agree with Lewiecki and colleagues that too few initial BMD tests are performed in older women. An appropriate response to our results would be for primary care physicians to substantially increase the number of initial tests in older women, then to tailor the subsequent BMD screening interval according to BMD T-score and age." |
| | 10 | There were other limitations not noted by the authors. Only clinical vertebral fractures were considered in the analysis, although undiagnosed morphometric vertebral fractures are common in patients with densitometric evidence of osteopenia and are associated with high morbidity (26). | Ref #26 is a prospective case series that followed women > 65 over 4 years and reported incidence of vertebral fracture and back pain/disability. It found that approx. 2/3 of new fractures were not diagnosed clinically, yet those patients still reported increased pain and disability. These fractures were diagnosed by lateral spine radiographs, which would not be indicated in the general population. Unclear how this relates to the recommended guidance, or how this suggests the need for more frequent monitoring. |
| | 11 | In a prospective cohort study of 671 postmenopausal women undergoing periodic spine imaging, 48% of vertebral fractures were found in women with T-scores between -1.0 and -2.5. With a morphometric vertebral fracture, they would be reclassified as having a clinical diagnosis of osteoporosis (27). Many of these patients would not have been identified in the study of Gourlay et al. | Ref #27 is a prospective case series of 671 postmenopausal women followed over 9 years. This study found that women who were osteopenic had an increased risk of fracture over that time period, and risk was also increased with age, prior fracture and high bone turnover |

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| | | | markers. There is no comment in the article regarding reclassification of these women as having osteoporosis. WHO criteria and NOF guideline list only T-score as criteria. |
| | 12 | In making treatment decisions in clinical practice, it is imperative to consider risk factors for fracture in addition to the femoral neck and total hip T-score. Gourlay et al., for example, did not measure lumbar spine BMD. Low lumbar spine BMD is associated with increased fracture risk at all skeletal sites (28). Moreover, lumbar spine T-score may be ≤ -2.5 even if the femoral neck or total hip T-score is > -2.5 . Without tracking lumbar spine BMD, Gourley et al. may have underestimated the number of individuals who progressed to osteoporosis during the study. Most importantly, with its singular focus on BMD, the study did not capture those patients with osteopenia who by the FRAX fracture risk assessment would have been at high risk for fracture and therefore warrant drug therapy. It would be grossly inappropriate to use the Gourlay et al study to set guidelines for frequency of BMD testing in the vast majority of clinical practice patients. | The abstract of Ref #28 states this was a prospective case series of 8,134 women > 65 followed 0.7 years and found the risk of fracture inversely related to BMD at all sites of measurement (proximal femur, spine, calcaneus, distal radius, proximal radius), and that none were more predictive than others. Does not appear to support contention that spine BMD needs to be tracked in addition to or instead of hip BMD. While the Gourlay article only evaluated BMD, again, no other evidence has been identified or provided that provides evidence supporting a different testing interval. |
| | 13 | NICE guidelines- These guidelines were developed through economic modeling of circumstances in the UK, where healthcare priorities and resources are quite different than in the US. This modeling used economic assumptions, including fracture-related medical expenses, that are uncertain even in the UK, and clearly not applicable in the US. FRAX in the UK was calibrated using country-specific fracture prevalence rates and mortality statistics that are not the same as in the US. There is controversy regarding the NICE guidelines amongst healthcare providers in the UK. As with all guidelines, NICE recognize that healthcare decisions should be individualized according the needs each patient. | HTAS does not disagree that modeling and economic assumptions in the UK may not apply perfectly to the US setting, but evidence to support an alternative testing schedule has not been provided. HTAS is familiar with controversy over testing guidelines, and while it is ideal for healthcare decisions to be individualized, that does not eliminate the need for a population-based coverage decision. |
| | 14 | Recommendations. It is my opinion that the proposed HERC Coverage Guidance, while well intentioned, is not sufficiently clear for clinical use, and that it would not be in the best interests of the citizens of Oregon to implement as it is. I think Oregon could do no better than to adopt the NOF guidelines for BMD testing and frequency of testing, allowing for physicians to individualize patient care decisions as needed. There are a number of minor formatting issues that should be corrected according to standard nomenclature established by the International Society for Clinical Densitometry (29). Change “DEXA” to “DXA,” which is the preferred acronym. Be consistent in using “T-score” and not other forms, such as “T score,” and express T-scores to one decimal place not two. Note that “advanced osteopenia” is not a recognized diagnostic category and should not be used; it was presented by the authors of the Gourlay et al study for use in their publication but has no established definition. | Some formatting corrections have been made, thank you. The use of 2 decimal points has been preserved, as this is directly from the evidence source. “Advanced osteopenia” is not deleted, as it is a helpful description of the T-score value 2.0 to 2.49. HTAS does not believe the NOF guidelines are sufficiently evidence-based for adoption. |

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