Citation: BoneKEy Reports **3**, Article number: 544 (2014) | doi:10.1038/bonekey.2014.39

www.nature.com/bonekey

COMMENTARY

Pre-screening young postmenopausal women for BMD testing

John A Kanis[1], Nicholas C Harvey[2] and Eugene McCloskey[1]

[1]Centre for Metabolic Bone Diseases, University of Sheffield Medical School, Sheffield, UK. [2]MRC Lifecourse Epidemiology Unit, University of Southampton, Southampton, UK.

BoneKEy Reports **3**, Article number: 544 (2014) | doi:10.1038/bonekey.2014.39; published online 11 June 2014

Commentary on: Crandall CJ, Larson J, Gourlay ML, Donaldson MG, LaCroix A, Cauley JA, Wactawski-Wende J, Gass ML, Robbins JA, Watts NB, Ensrud KE. Osteoporosis screening in postmenopausal women 50–64 years-old: Comparison of U.S. Preventive Services Task Force Strategy and two traditional strategies in the women's health initiative. *J Bone Miner Res* (e-pub ahead of print 16 January 2014; doi:10.1002/jbmr.2174).

Screening for osteoporosis has long been a contentious issue and is not widely recommended. An important exception is in North America where BMD testing by measurement of bone mineral density (BMD) is widely advocated, although less widely practised. The principal indication for treatment in the United States is in women with a BMD T-score of -2.5 s.d. or less, apart from women with a history of a prior spine or hip fracture (in whom treatment is recommended). To attain this goal, the National Osteoporosis Foundation (NOF) and the United States Preventive Services Task Force (USPSTF) advise BMD testing in women from the age of 65 years and recommend treatment if BMD is in the range for osteoporosis.[1,2] In younger women aged 50–64 years, the NOF recommends BMD testing based on the risk factor profile, for which the USPSTF recommends the use of the World Health Organization's Fracture Risk Assessment Tool, FRAX,[3] as a pre-screening tool.[2] A BMD test is recommended in women with a 10-year probability of a major fracture (measured without BMD) of 9.3% or higher. The figure of 9.3% is equivalent to that of a 65-year-old white woman with no other FRAX clinical risk factors and a body mass index of 25 kg m^{-2} (http://www.shef.ac.uk/FRAX/).

Against this background, Crandall and her colleagues have compared the USPSTF recommendations for younger women with two tools for the identification of low BMD, neither of which are included in the NOF or USPSTF guidance.[4] These comprised the Osteoporosis Self-Assessment Tool (OST) and Simple Calculated Osteoporosis Risk Estimation Tool (SCORE).[5,6] OST is calculated from weight and age, whereas SCORE uses six clinical risk factors (race, rheumatoid arthritis, history of non-traumatic fracture, age, prior oestrogen therapy and weight). The study examined 5167 postmenopausal women aged 50–64 years recruited to a component of the Women's Health Initiative.[7]

The principal finding, summarised in **Table 1**, was that the FRAX-based (USPSTF) strategy had a somewhat higher specificity but much lower sensitivity than SCORE or OST for the identification of individuals with a femoral neck T-score of $\leqslant -2.5$ s.d.. The low sensitivity with the FRAX cut-off means that two-thirds of women with a BMD in the range of osteoporosis would be missed. Sensitivity would be raised to $\sim$90% with a FRAX cut-off probability of around 4% rather than 9.4%.

These findings are not surprising. In a meta-analysis of the performance characteristics of OST for the prediction of osteoporosis, sensitivity was high in women at 83% (95% confidence interval (CI) = 81–84%) with a specificity of 63% (95% CI = 62–64%).[3] Although lower than the sensitivity, the moderately high specificity provides opportunities for cost savings by excluding patients who do not need a BMD assessment. In one study, it was estimated that $\sim$55% of BMD tests would be saved, compared with 100% BMD testing with mass screening.[8]

The headline from Reuters says it all: 'Osteoporosis Screening Strategies Suboptimal for Younger Postmenopausal Women'.[9] It is difficult not to agree with the headline but this accord is not based on the analysis of Crandall *et al.*, thorough though this may be. A clue lies in the discussion section of the paper by Crandall *et al.*, in which the authors state that 'The objective of screening is to identify postmenopausal women with T-scores of -2.5 s.d. or lower'. In contrast, a more apposite view would be that the objective of screening is to identify postmenopausal women at a high risk of fracture. Indeed, although densitometrically defined T-score has historically constituted the sole basis of osteoporosis disease definition, it may be more appropriately considered in this context as one of the many risk factors for the clinically important outcome of fragility fracture. The authors adopt their view 'because pharmacologic treatment to prevent fractures has been demonstrated to be effective in this group'. This ignores the wealth of evidence that treatments are effective in high-risk patients unselected by BMD.[10] In this context, it is ironic that the Women's Health Initiative demonstrated the effectiveness of hormone replacement treatment on fracture outcomes in women unselected by BMD.[11]

Table 1 Sensitivity, specificity and AUC using three assessment tools for the identification of individuals with femoral neck T-score $\leqslant -2.5$ s.d. (extracted from Table 3[4])

Tool	*Cut-off*	*Sensitivity*	*Specificity*	*AUC*
FRAX	9.4%	33.3	86.4	0.60
SCORE	>7	74.1	70.8	0.72
OST	<2	79.3	70.1	0.75

Abbreviations: AUC, area under the receiver operating characteristic curve; FRAX, Fracture Risk Assessment Tool; OST, Osteoporosis Self-Assessment Tool; SCORE, Simple Calculated Osteoporosis Risk Estimation Tool.

The logic behind the USPSTF probability threshold of 9.3% is as follows. If a BMD test is indicated at the age of 65 years (and above), then a BMD test is indicated in younger postmenopausal women in whom the fracture probability exceeds that of a 65-year-old woman. The 10-year probability of a 65-year-old Caucasian woman (BMI 25 kg m^{-2}) is 9.3%, hence the 9.3% threshold. The same logic is applied in the development of guidelines for assessment in many European countries. Thus, many guidelines recommend that women with a prior fragility fracture may be considered for intervention without the necessity for a BMD test (other than to monitor treatment).[12] From this, a prior fracture may be considered to carry a sufficient risk that treatment can be recommended. For this reason, the intervention threshold in women without a prior fracture is set at the age-specific fracture probability equivalent to women with a prior fragility fracture; it necessarily rises with age from a 10-year probability of 8–33% in the UK.[13] In other words, the intervention threshold is set at the 'fracture threshold'. The same principles have been applied to European guidance and in the management of glucocorticoid-induced osteoporosis.[12,14]

In brief, the probability threshold of 9.3% used by the USPSTF is logical, but may be deemed inappropriate if the 'The objective of screening is to identify postmenopausal women with T-scores of -2.5 s.d. or lower'.[4] We would argue that the USPSFT is correct in aiming to identify women at a high risk of fracture, the purpose for which FRAX was designed, rather than those individuals with BMD-defined osteoporosis. If the intention of screening is to identify women at a high risk, then a fracture risk assessment algorithm is the appropriate tool. In this context, FRAX outperforms OST or SCORE for fracture prediction.[3] Given that in the United States treatment is recommended in women with a prior spine or hip fracture, as is the case in many countries, a starting approach is to base screening thresholds on such fracture probabilities. In this context, BMD tests are best reserved for individuals who lie close to an intervention threshold, an approach that makes the best use of available scanning resources.

Conflict of Interest

The authors declare no conflict of interest.

References

1. National Osteoporosis Foundation 2013. NOF's newly revised 2013 Clinician's Guide to Prevention and Treatment of Osteoporosis http://www.nof.org/hcp/practice/practice-and-clinical-guidelines/clinicians-guide. Accessed on 18 February 2013.
2. United States Preventive Services Task Force. Screening for osteoporosis: U.S. preventive services task force recommendation statement. *Ann Intern Med* 2011;**154**:356–364.
3. Kanis JA, on behalf of the World Health Organization Scientific Group. Assessment of osteoporosis at the primary health-care level. Technical Report. World Health Organization Collaborating Centre for Metabolic Bone Diseases, University of Sheffield, UK 2007.
4. Crandall CJ, Larson J, Gourlay ML, Donaldson MG, Lacroix A, Cauley JA *et al.* Osteoporosis screening in postmenopausal women 50-64 years-old: Comparison of U.S. Preventive Services Task Force strategy and two traditional strategies in the Women's Health Initiative. *J Bone Miner Res.* (e-pub ahead of print 16 January 2014; doi:10.1002/jbmr.2174).
5. Lydick E, Cook K, Turpin J, Melton M, Stine R, Byrnes C. Development and validation of a simple questionnaire to facilitate identification of women likely to have low bone density. *Am J Manag Care* 1998;**4**:37–48.
6. Koh LK, Sedrine WB, Torralba TP, Kung A, Fujiwara S, Chan SP *et al.* A simple tool to identify Asian women at increased risk of osteoporosis. *Osteoporos Int* 2001;**12**:699–705.
7. Women's Health Initiative Study Group. Design of the Women's Health Initiative clinical trial and observational study. *Control Clin Trials* 1998;**19**:61–109.
8. Geusens P, Hochberg MC, van der Voort DJ, Pols H, van der Klift M, Siris E *et al.* Performance of risk indices for identifying low bone density in postmenopausal women. *Mayo Clin Proc* 2002;**77**:629–637.
9. Boggs W 2014, Osteoporosis screening strategies suboptimal for younger postmenopausal women. Reuters health information www.medscape.com, 28 February 2014. Accessed on 1 March 2014.
10. Kanis JA, McCloskey E, Johansson H, Oden A, Leslie WD. FRAX® with and without BMD. *Calcif Tissue Int* 2012;**90**:1–13.
11. Cauley JA, Robbins J, Chen Z, Cummings SR, Jackson RD, LaCroix AZ *et al.* Effects of estrogen plus progestin on risk of fracture and bone mineral density: the Women's Health Initiative randomized trial. *JAMA* 2003;**290**:1729–1738.
12. Kanis JA, McCloskey EV, Johansson H, Cooper C, Rizzoli R, Reginster J-Y *et al.* European guidance for the diagnosis and management of osteoporosis in postmenopausal women. *Osteoporos Int* 2013;**24**:23–57.
13. Kanis JA, McCloskey EV, Johansson H, Strom O, Borgstrom F, Oden A. Case finding for the management of osteoporosis with FRAX—assessment and intervention thresholds for the UK. *Osteoporos Int* 2008;**19**:1395–1408.
14. Lekamwasam S, Adachi JD, Agnusdei D, Bilezikian J, Boonen S, Borgström F *et al.* A framework for the development of guidelines for the management of glucocorticoid-induced osteoporosis. *Osteoporos Int* 2012;**23**:2257–2276.