**Medical Policy Manual** Radiology, Policy No. 48

# *Screening for Vertebral Fracture or Fracture Risk with Dual X-ray Absorptiometry (DXA)*

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## IMPORTANT REMINDER

Medical Policies are developed to provide guidance for members and providers regarding coverage in accordance with contract terms. Benefit determinations are based in all cases on the applicable contract language. To the extent there may be any conflict between the Medical Policy and contract language, the contract language takes precedence.

PLEASE NOTE: Contracts exclude from coverage, among other things, services or procedures that are considered investigational or cosmetic. Providers may bill members for services or procedures that are considered investigational or cosmetic. Providers are encouraged to inform members before rendering such services that the members are likely to be financially responsible for the cost of these services.

## DESCRIPTION

Dual x-ray absorptiometry (DXA) makes it possible to screen for vertebral fractures and fracture risk while measuring bone mineral density (BMD).

## MEDICAL POLICY CRITERIA

**Note:** This policy addresses only dual x-ray absorptiometry (DXA) for the routine screening of asymptomatic patients with or without osteoporosis for vertebral fractures. It does not address the diagnostic assessment of symptomatic patients, routine bone mineral density screening, or DXA to determine body composition.

I. Screening for vertebral fractures using dual x-ray absorptiometry (DXA) as a stand-alone procedure or in addition to standard bone mineral density studies is considered **investigational**.
II. Screening for vertebral fracture risk using trabecular bone score (TBS) is considered **investigational.**

*NOTE: A summary of the supporting rationale for the policy criteria is at the end of the policy.*

## CROSS REFERENCES

1. Whole Body Dual X-Ray Absorptiometry (DXA) to Determine Body Composition, Radiology, No. 41

## BACKGROUND

DXA imaging may also be referred to as bone densitometry, morphometric x-ray absorptiometry (MXA), Instant Vertebral Assessment (IVA) (Hologic), Radiographic Vertebral Assessment (RVA) (Hologic), or Dual Energy Vertebral Assessment (DVA™) previously known as Lateral Vertebral Assessment™ (LVA) (GE Lunar Medical Systems).

Trabecular bone score (TBS) is a diagnostic software tool that can analyze the internal structure of the lumbar spine and is used in conjunction with a DXA imaging scan. TBS uses standard DXA lumbar spine images to measure the structure of trabecular bone, providing an additional metric to BMD assessments to assess fracture risk. The TBS is derived from the texture of the DEXA image and has been shown to be related to bone microarchitecture and fracture risk.

Vertebral fractures are highly prevalent in the elderly population, and epidemiologic studies have found that these fractures are associated with an increased risk of future spine or hip fractures, independent of bone mineral density. For example, several studies have reported that asymptomatic vertebral fractures may be present in up to 20% of postmenopausal women who have normal BMD measurements. Only 20%–30% of vertebral fractures are recognized clinically; the rest are discovered incidentally on lateral spine radiographs, considered the gold standard for diagnosing vertebral fracture. Lateral spine x-rays, however, have not been recommended as a component of risk assessment for osteoporosis because of the cost, radiation exposure, and the fact that the x-ray would require a separate procedure in addition to the bone mineral density study. Thus, the population for which DXA is most relevant includes those patients who might benefit from treatment but would not be considered for treatment based on current BMD standards alone.

The semiquantitative system of Genant is commonly used for grading vertebral deformities. The location of the deformity within the vertebrae may also be noted. For example, if only the mid-height of the vertebrae is affected, the deformity is defined as an endplate or biconcave deformity; if both the anterior and mid-heights are deformed, it is a wedge deformity; and if the entire vertebrae is deformed, it is classed as a crush deformity.

| **Genant Semi-Quantitative Grading System for Vertebral Deformity** | |
|---|---|
| **Grade/Fracture** | **Reduction in vertebral height** |
| Grade 0-0.5/no fracture | **< 20%** |
| Grade I/mild fracture | **20%–25%** |
| Grade II/moderate fracture | **25%-40%** |
| Grade III/severe fracture | **>40%** |

### Regulatory Status

Many DXA devices have received 510(k) marketing clearance from the U.S. Food and Drug Administration (FDA), including but not limited to Hologic's IVA and GE's DVA noted above. To perform vertebral fracture assessment on the DXA devices, additional software is needed and 510(k) marketing clearance from the FDA is required. Multiple TBS software programs have

received 510(k) clearance from the U.S. FDA including OsDx Hip BMD System, TBS iNsight, and TBS 3.1.

## EVIDENCE SUMMARY

For symptomatic patients, vertebral fractures may be diagnosed with radiography, CT or MRI, if necessary, depending on the clinical scenario. As noted above, the population for which dual x-ray absorptiometry (DXA) screening for vertebral fractures is most relevant includes those patients who would not be considered for treatment based on current bone mineral density (BMD) measurements alone (i.e., patients without osteoporosis and without symptoms of vertebral fractures). Further, a benefit of treatment in reducing risk of future fractures also needs to be demonstrated in this patient population. To demonstrate that screening for vertebral fractures using DXA improves patient selection and health outcomes, well-designed randomized controlled trials (RCTs) are necessary. Studies should compare those patients screened for vertebral fractures using DXA as a stand-alone procedure or using DXA in addition to standard bone mineral density studies, with those patients screened with standard bone mineral density studies alone.

### TECHNOLOGY ASSESSMENTS

The 2005 BlueCross BlueShield (BCBSA) Technology Evaluation Center (TEC) Assessment concluded that the available evidence was insufficient to assess from the impact of vertebral assessment using DXA compared to BMD screening alone.[1] As there was no direct evidence, the conclusions in the 2005 technology assessment were based on examination of indirect evidence:

1. What is the accuracy of vertebral assessment with DXA in identifying vertebral fractures?

   According to the proposed use of vertebral assessment, identifying vertebral fractures among those who otherwise might not be treated, such as those without osteoporosis, is an important benefit of the test. However, there is a lack of evidence that the test is very accurate in detecting fractures among those without osteoporosis.

   Some evidence exists regarding the diagnostic performance of vertebral assessment. In studies ranging in sample size from 66 to 161 patients, the sensitivity for detecting vertebral fractures ranged from 54% to 72% using the vertebrae as the unit of analysis, and 77% to 95% using the patient as the unit of analysis. Specificities ranged from 94% to 99% using the vertebrae as the unit of analysis, and 88% to 94% using the patient as the unit of analysis. However, the patient populations in which these characteristics were assessed may not generalize to the population most relevant for detection of vertebral fractures. Two of the studies included only patients with known osteoporosis.[2-4] One study that showed the highest sensitivity may be biased by selective verification.[5] Another study, which included a sample not known to be osteoporotic, showed the lowest sensitivity for fracture at 54%.[6]

2. Does vertebral assessment with DXA identify patients who are appropriate candidates for treatment who would not otherwise be identified?

   Conclusions about the utility of the test, given its diagnostic characteristics, must then be placed in context of the clinical use of the test in making treatment decisions.[2, 3] More

recent publications of large trials of pharmacologic treatments for osteoporosis appear to show treatment benefits for subjects with osteopenia. Thus, the threshold for treatment is uncertain, although it is recognized that knowledge of a prevalent vertebral fracture would likely alter any specified threshold for treatment. However, the performance of vertebral assessment in relevant screening populations should be definitively established before routinely used for treatment decisions. Although, it may be possible to project patient outcomes when treatment is based on results of these tests, taking into account possible negative consequences of inappropriate treatments due to either false-negative or false-positive findings.

In summary, the TEC Assessment concluded that the evidence supporting the use of vertebral assessment was not strong enough to allow conclusions about its treatment effect on health outcomes.

## DIAGNOSTIC ACCURACY

### Systematic Reviews

In 2016, Lee published a systematic review of studies on the diagnostic accuracy of vertebral fracture assessment (VFA) in postmenopausal women and elderly men.[7] The investigators compared the diagnostic accuracy of vertebral fracture assessment (VFA) with that of spinal radiography for identification of vertebral fractures (VFs), analyzing sensitivity and specificity in twelve studies. Of the twelve included studies, only five studies were considered to have low risk of bias. The sensitivity and specificity of five studies with low risk of bias were 0.70-0.84 and 0.96-0.99, respectively, indicating that VFA has moderate sensitivity and high specificity for detecting VF when compared with spinal radiography. The investigators concluded that the present findings are insufficient to assess whether spinal radiography should be replaced by VFA.

Randomized Controlled Trials

No RCTs evaluating the diagnostic accuracy of DXA for vertebral fractures were identified.

Nonrandomized Studies

A number of nonrandomized studies have been published since the systematic review above.

A 2014 study by Kanterewiez[8] collected data on a population-based cohort of 2968 postmenopausal women in Spain between the ages of 59 and 70 years.(7) A total of 127 women (4.3%) had a vertebral fracture according to VFA. Among these, 48.0% had osteoporosis and 42.5% had osteopenia. Moreover, 42.5% had previous fragility fractures and 34.6% had a first-degree family history of fractures. Thus, VFA could potentially identify additional women who would be eligible for fracture prevention therapy according to NOF guidelines (i.e., women who did not have osteoporosis, osteopenia plus a 10-year fracture risk, or other risk factors). The authors did not attempt to define this subgroup (e.g., they did not report data on women with normal BMD and other risk factors.)

Two studies, published in 2016 and 2017, evaluated DXA imaging versus conventional radiography for vertebral fracture assessment in children.[9, 10] Crabtree compared results from DXA VFA and morphometric analysis (MXA) with spinal radiograph assessment (RA) obtained the same day in 80 children.[9] Agreement between DXA and RA was adjudicated by three specialists, and agreement between MXA and RA was adjudicated by four specialists.

Altogether, there were 121 mild, 44 moderate, and 16 severe fractures identified. Moderate agreement was found between DXA and RA using the Cohen kappa score (kappa 0.630-0.687), but this was substantially lower for MXA and RA (0.361-0.406). The sensitivity/specificity for detecting moderate or severe fractures was 81.3%/99.3% for VFA and 62.5%/99.2% for MXA in this study. The study by Adiotomre compared DXA to RA performed the same day in 250 children.[10] These were scored independently by three radiologists. The sensitivity/specificity for diagnosis of vertebral fractures requiring treatment was 70%/97% for DXA and 74%/96% for RA. The results of these studies indicate that DXA and RA perform similarly for vertebral fracture assessment in children.

Deleskog (2016) compared DXA VFA with x-ray in a retrospective study of 35 patients with severe osteoporosis that were referred to a clinic for teriparatide treatment.[11] The semiquantitative approach was used to diagnose VF based on DXA and x-ray imaging independently. Primary image interpretation was performed by the same technician for both sources, and these were reviewed by a radiologist and endocrinologist for final adjudication. In this high-risk group, a total of 180 fractures were identified, for an average of 5.1 fractures per patient. The sensitivity/specificity of DXA VFA was 75.5%/86.7%, using x-ray diagnosis as the reference. There was a decrease in VFA sensitivity from the lumbar to the thoracic level, and only fractures from Th11-L3 were consistently identified. The authors concluded that VFA did not perform as well as x-ray for analysis of vertebrae in the upper spine.

Section Summary

Several studies and a 2016 systematic review have compared VFA with radiography. The sensitivity of VFA reported in these studies was variable. Some have reported relatively low sensitivities in the 50-60% range while others, particularly more recent studies, have reported sensitivities of over 90%. The specificity in these studies has been higher, with some studies reporting specificities of >95%. However, at least one study reported a specificity of 62%. Moreover, studies tended not to present diagnostic accuracy rates separately for individuals without osteoporosis, although two studies have been tested VFA in children. Due to the variability in these results and the lack of stratified analyses, it is not possible to determine the sensitivity and specificity of VFA for vertebral fractures with certainty, either for patients as a whole or for the subset of patients without osteoporosis.

## EVIDENCE THAT VERTEBRAL ASSESSMENT IDENTIFIES CANDIDATES FOR TREATMENT WHO WOULD NOT OTHERWISE BE IDENTIFIED

Vertebral fracture assessment could identify additional candidates for treatment if individuals with vertebral fractures did not fall into one of the other categories eligible for treatment. No studies were found that specifically dealt with the question of whether VFA would identify candidates for medication treatment who would not otherwise have been identified, but several studies addressed this issue to some extent. Representative studies are described below.

Yang (2020) conducted a systematic review and meta-analysis of 28 studies evaluating detection of vertebral fractures via VFA with DXA in asymptomatic postmenopausal women.[12] Study sample sizes ranged from 63 to 5156 and mean age ranged from 59.5 to 86.2 years. Among women who had prevalent vertebral fractures,11.1-43% had osteopenia and 3.6-32% had normal BMD. The weighted pool prevalence of VFA-detected vertebral fractures was 28% (95% CI, 23% to 32%) with a high degree of heterogeneity.

Greendale (2016) used data from the Study of Women's Health Across the Nation, a multi-site cohort study, to evaluate the performance of DXA vertebral morphometry (VM) measurement and gather information about the epidemiology of vertebral deformities.[13] Between 2004 and 2007, the Hologic QDR 4500A was used to measure VM in 1446 women, and a follow-up VM in 2012-2013 was acquired in 1108 (77%) of these subjects. The mean age of the women at baseline VM was 54 years (SD 2.7). BMD of the lumbar spine and femoral neck were measured annually. VM measurements were read by a single research radiologist. The proportion of readable vertebral bodies was lowest in the cranial region and was between 43% and 63% for levels T4-T6. Higher BMI was correlated with fewer readable vertebrae. At baseline, 46 of the women (3.2%) had a vertebral deformity, and this was associated with decreased BMD and older age. The majority (67%) were grade 1 deformities, defined as "approximately 20–25% reduction in anterior, middle, and/or posterior height and a reduction of area 10–20%". After an average follow-up of 6.8 years, the incidence of new vertebral deformities was 1.72 per 1,000 person/years for women younger than 60 years of age at baseline and 2.09 per 1,000/person years for women aged 60 or older at baseline.

Mrgan (2013) published a retrospective study in Denmark evaluating VFA with BMD in 3275 patients presenting for osteoporosis screening or evaluation of anti-osteoporotic medication; 85% were female.[14] Vertebral fractures were found on VFA in 260 patients (7.9%). Of these, 156 patients (4.8% of the total sample) had osteoporosis (i.e., BMD at least -2.5) and 104 (3.2% of the total sample) did not have osteoporosis according to BMD. The data suggest that up to 40% (104 of 250) of patients with vertebral fractures identified would be eligible for treatment according to NOF guidelines and might not have been identified if DXA alone were used. The proportion is likely lower than 40% because some of the patients may have had osteopenia and other risk factors that would lead to their eligibility for treatment.

Jager (2011) evaluated 2424 consecutive individuals (65% female) referred for BMD for a variety of reasons at a single center in the Netherlands.[15] Participants underwent VTA with BMD during the same session using a Hologic Discovery A densitometer. Vertebral fractures (reduction in height of at least 20%) were detected in a total of 541 (22%) of patients. The prevalence of vertebral fractures was 14% (97/678) in individual with normal BMD and 21% (229/1100) in patients with osteopenia. The vertebral fractures were previously unknown in 74% of patients with normal BMD and 71% of patients with osteopenia. Questionnaires were sent to 942 physicians, with a response rate of 50%. Of these 468 responses, 323 (69%) of physicians reported that VFA findings had no impact on patient management, 100 (21%) reported some impact, 29 (6%) reported a large impact and there were 16 (3%) unknown responses. A total of 58 responses indicated that VFA findings impacted medication decisions.

A study by Van den Berg (2011) included 566 women 50 years of age or older who had clinical risk factors for fracture but who were not being treated for osteoporosis and had not previously been diagnosed with a vertebral fracture.[16] Women underwent DXA and VTA screening with a Hologic W DXA system. A total of 174 (31%) had one or more moderate or severe vertebral fractures (height reduction of 25% or more). Mild vertebral fractures were not reported. Of the 174 women with vertebral fractures, 44 (25%) were found to have osteoporosis and therefore would have been eligible for treatment based on their BMD alone. However, the remaining 130 (75%) women with vertebral fractures had normal BMD (n=32) or osteopenia (n=43). It is not known how many of the women with osteopenia would have otherwise been considered potential candidates for treatment due to the combination of low bone mass and other risk factors. Among women with vertebral fractures, 17 (10%) used glucocorticoids, 91 (52%) had a

previous fracture before age 50 and 39 (22%) had a first-degree relative with a hip fracture. The authors did not report women's overall risk of fracture using the FRAX model.

Renui (2017) assessed the prevalence of vertebral fracture by DXA in patients presenting to a large UK hospital with a non-hip, non-vertebral fragility fracture.[17] Between 2012 and 2015, 2180 patients aged 50 years or older were referred for a DXA scan. Those patients with a known VF, previous VFA, DXA imaging suggestive of a VF, or a BMD less than or equal to 2.5 standard deviations (SD) below the young adult mean at either hip or spine received VFA, for a total of 567 study subjects (88.3% women). There were 143 patients (25.2%) with a VF diagnosed by VFA, and 49.5% of these patients also had a BMD measurement consistent with osteoporosis. These results indicate that the use of BMD values alone to select patents for VFA would miss a substantial number of patients with VFs.

Sullivan (2011) evaluated the prevalence of vertebral fracture in men at increased risk of bone loss who were undergoing DXA screening.[18] The study included 116 men with non-metastatic prostate cancer who had been taking androgen deprivation therapy for at least six months. There were 37 (37%) men found to have normal BMD on DXA; nine (24%) of these had at least one VF. In addition, 67 (59%) of men were found to have low BMD/osteopenia; 23 (34%) had at least one vertebral fracture. A total of 32 of the 104 (31%) men with normal or low BMD had a least one vertebral fracture. Patients also underwent radiographic confirmation of fractures. Compared with radiography, the sensitivity of VFA was 100% and the specificity was 95%. Thus, according to the NOF recommendations, 32 men (28% of the sample) with normal or low bone density would be recommended for osteoporosis treatment based on their radiologically identified vertebral fracture. Androgen deprivation therapy is not currently included in the WHO absolute fracture risk model so those men with osteopenia and ADT would not have been recommended to receive treatment.

Jager (2010) assessed the impact of VFA on the Canadian risk classification system.[19] The study reported on data collected on VFA with densitometry in the Netherlands, and the article was written by researchers from the Netherlands and Canada. The study included 958 individuals at least 18 years-old who had been referred for BMD measurements. Their mean age was 53 years; 609 (64%) were women, and 93 (10%) were already known to have a vertebral fracture. In 937 of the 958 patients (98%), VFA was considered technically adequate. Using VFA, a vertebral fracture was identified in 244 of 937 (26%) of those with an adequate scan. This included 18% of the 257 patients found on DEXA to have normal BMD, 23% in the 404 patients with osteopenia, and 29% of the 275 patients with osteoporosis. Using the Canadian risk classification tool categorizing fracture risk according to age, gender, and BMD T-score, the proportion of patients who would have been categorized as low, moderate, and high risk was 650 (68%), 184 (19%), and 124 (13%), respectively. After taking VFA into account, 133 patients with a low risk who were found to have one or more vertebral fractures would have been moved to the moderate-risk class. Moreover, 59 of the moderate-risk patients were found to have one or more vertebral fractures, which moved them to the high-risk category. In total, 192 patients (20% of the cohort) moved up one risk class. The study did not compare the VFA findings to a reference standard and did not evaluate the effect of treatment on preventing fracture in patients placed into risk categories that used data from VFA with densitometry.

**Section Summary**

Routine use of VFA with DXA will identify substantial numbers of individuals with previously unrecognized vertebral fractures. Many of these vertebral fractures are found in individuals without osteoporosis. Since screening for vertebral fractures is not currently part of the recommended workup for osteoporosis, it is not clear how to combine a positive result on VFA with other risk factors to make management decisions.

## EVIDENCE ON EFFECTIVENESS OF PHARMACOLOGIC TREATMENT IN PATIENTS WITH LOW BONE MASS AND VERTEBRAL FRACTURE

Bisphosphonates (e.g., alendronate) decrease bone resorption and are the major class of drugs now used to treat osteoporosis. In several large, multicenter trials in osteoporotic women, treatment with alendronate has been shown to increase bone density by 5–10% over a three-year period. These trials were not designed a priori to assess efficacy according to BMD categories or according to baseline vertebral fracture status. However, several subgroup analyses have been published examining the effectiveness of treatment in patients with low bone mass and/or vertebral fractures.

The original report from one of the Fracture Intervention Trial (FIT) study groups was the first large multicenter study comparing the effects of treatment between osteoporotic and women with low bone mass without existing vertebral fractures using the revised National Health and Nutrition Examination Survey (NHANES) cutoffs.[20] This trial randomly assigned 4,432 women to alendronate or placebo and analyzed the treatment group in 3 BMD categories (less than -2.5 standard deviation (SD); -2.0 to -2.5 SD; and -1.6 to -2.0 SD below the mean). Women with a BMD less than -2.5 SD had a statistically significant reduction in clinical and vertebral fractures over four years. The relative risk (RR) for all clinical fractures among patients with a BMD less than -2.5 SD was 0.6 (95% confidence interval [CI]: 0.5–0.8). There was no significant reduction in all clinical fractures for women with higher BMD values (RR 1.1, 95% CI: 0.9–1.4), suggesting no benefit among patients with low bone mass or normal BMD.

Quandt (2005) reanalyzed the FIT study analyzing data for the outcome of both clinical vertebral fractures (symptomatic and diagnosed by physician) and radiographically detected (assessed at surveillance intervals) vertebral fractures.[21] A total of 3,737 women at least two years' post-menopausal with low bone mass (T-score between -1.6 and -2.5) were included in the analysis. Among the women with low bone mass and existing radiographically detected vertebral fractures (n=940), the rate of subsequent clinical vertebral fractures were 6 (a rate of 43 per 10,000 person-years of risk) in the alendronate group and 16 (124 per 10,000 person-years of risk) in the placebo group. Alendronate treatment compared to placebo was accompanied by a RR of 0.3 (95% CI: 0.1–0.8) for clinical vertebral fractures and a RR of 0.5 (95% CI: 0.3–0.8) for radiographically detected fractures. Similar RR estimates were found for women having low bone mass without vertebral fractures, but absolute risks were lower (12 versus 81 fractures/10,000 person-years for those without and with baseline fractures, respectively).

Kanis (2005) reanalyzed data on 1,802 women at least five years' postmenopausal from the Vertebral Efficacy with Risedronate Therapy (VERT) trials who were identified on the basis of a prior radiographically detected vertebral fracture regardless of BMD and had radiographs available at baseline and three years.[22] Overall, there was a significantly lower rate of a new vertebral fracture in women with prior vertebral fracture randomly assigned to treatment with risedronate compared to placebo (14.5% vs. 22.3%, respectively; $p<0.001$). In the group with a T-score greater than -2.5, the rate of new femoral neck fractures was 50 of 519 (11%) in the

risedronate group and 71 of 537 (15.5%) in the placebo group (p=0.049). In the osteoporotic group, those with a T-score -2.5 or lower, the rate of new femoral neck fracture was 53 of 355 (18.7%) in the risedronate group and 92 of 318 (33.4%) in the placebo group (p<0.001). Findings were similar when the T-score at the most severe skeletal site (femoral neck or lumbar spine) was used for stratification.

A limitation of the studies described above is that they are post-hoc subgroup analyses, which are generally considered to be exploratory. In addition, vertebral fracture screening was performed using radiography rather than VFA software. Advantages of the studies are that the two sub-analyses had large sample sizes and used data from well-conducted randomized trials. The analyses included the population of interest (those with low bone density and a baseline vertebral fracture), although only in postmenopausal women; men and pre- and perimenopausal women were not included.

No RCTs were identified that evaluated the efficacy of bisphosphonate treatment in men with vertebral fractures and low bone density. Several trials have evaluated whether bisphosphonate treatment increases BMD in men at risk for bone loss (e.g., on androgen deprivation therapy).[23, 24] However, vertebral fractures were not assessed and therefore conclusions cannot be drawn about the potential added benefit of VFA in addition to densitometry in at-risk men.

### Section Summary

Evidence from the FIT and VERT studies suggests that treatment of patients with low bone mass (but not osteoporosis) reduces further fractures. However, a limitation of the FIT and VERT studies is that they are post-hoc subgroup analyses, which are generally considered to be exploratory. In addition, vertebral fracture screening was done using radiography rather than VFA software. Advantages of the studies are that the two sub-analyses had large sample sizes and used data from well-conducted randomized trials. This evidence is insufficient to determine whether treatment of patients with low bone density and vertebral fractures improves outcomes.

## TRABECULAR BONE SCORE (TBS)

### Systematic Reviews

Shevoja (2023) published a SR and international expert consensus statement on the clinical utility of TBS and included a total of 48 studies (20 prospective cohort design studies for postmenopausal woman and males with osteoporosis and 28 mostly retrospective and cross-sectional studies relevant to secondary osteoporosis. Majority of the studies were conducted outside of the US. [25] They divided the outcomes into four topics:

1. Use of TBS in fracture risk predication in postmenopausal and males with osteoporosis - 18 studies included were prospective study design in men or women over the age of 40. Ten studies were conducted in postmenopausal women, five in men, and three in both men and women, with mean age ranging from 58 to 76 years. The incident fracture rates for major osteoporotic fractures (MOF, including hip) ranged from 1.2 to 14%, and for vertebral fractures, 3.5 to 35%. TBS was an independent predictor of incident fracture in 16 of 18 studies. For each SD reduction in TBS, the increased risk of incident fracture ranged from 19% to more than double. The combination of TBS and BMD significantly enhanced the

prediction of fracture risk compared to lumbar spine BMD in men and women, although, in one study, this was only significant in men.

2. Use of TBS for the initiation of treatment and monitoring of treatment effect in postmenopausal osteoporosis: 20 studies (prospective or intervention trial of an antiosteoporosis treatment in postmenopausal women, ≥ 6 months treatment duration - n ranging from 28 to 6985, treatment duration ranging from 6 months to 10 years. Studies included antiresorptive treatments anabolic treatments, and/or sequential treatment and/or treatment combinations.

    a. Collectively, the evidence indicates that bisphosphonates, SERMs and MHT are unlikely to result in TBS change as they act primarily to preserve bone microarchitecture, as confirmed by histomorphometric analyses. On the other hand, denosumab, a more potent antiresorptive agent, with a potential bone-forming effect, results in sustained, modest to large gains in TBS with extended treatment durations up to 10 years. They recommend that TBS in conjunction with BMD is useful for monitoring individual responses to denosumab, PTH/PTHrP analogue and romosozumab treatment.

3. Use of TBS in the prediction of fracture risk associated with secondary osteoporosis: 40 studies (seven prospective) met the eligibility criteria (prospective, retrospective, or cross-sectional studies, fracture as the primary outcome, in men and/or women aged ≥ 18 years). They concluded that TBS predicts fracture risk in type 2 diabetes, chronic kidney disease, glucocorticoid treatment, rheumatological diseases, independently of BMD and/or FRAX and the TBS was relatively unaffected by spinal changes.

4. Use of TBS for treatment monitoring in secondary osteoporosis: Twenty-eight studies met the eligibility criteria (prospective, retrospective cohort or case–control cross-sectional design; treatments associated with secondary causes of osteoporosis, or antiosteoporosis therapies in secondary osteoporosis; men and/or women, age ≥ 18 years) and thirteen studies included men. Only six were conducted in a US population. They concluded that TBS "adds value" when used with BMD for monitoring skeletal effects of aromatase inhibitors and glucocorticoids.

They conclude that TBS enhances fracture risk prediction in both primary and secondary osteoporosis, and across diverse races and ethnicities. Together with FRAX, the inclusion of TBS in conjunction with BMD can provide an improved global assessment of fracture risk, which considers the two pillars of fracture resistance (bone mass and bone microarchitecture) and CRFs. Where FRAX is not available, TBS alongside BMD provides a dual skeletal assessment of fracture risk, and the lowest BMD T-score-adjusted for TBS can be input into other fracture risk assessment tools. Limitations to these outcomes include heterogeneity of methodology and outcomes including different versions of the software applications, a variety of studies designs ranging from registry data to prospective cohort studies. Many of the authors have listed conflicts of interest including receiving payments from device and pharmaceutical companies.

A meta-analysis by McCloskey (2016) examined the TBS predicted fractured risk compared to the Fracture Risk Assessment Tool (FRAX)[26]. Researchers utilized data from 17,809 men and women from 14 cohort studies. Each participant had a baseline evaluation that included FRAX and TBS, and measured fracture outcomes during a follow-up (mean 6.7 years). Independent of FRAX score, TBS was a significant, independent predictor for fracture. This data shows

initial support for the use of TBS to improve the accuracy of fracture risk, but additional research is needed to identify if assessing TBS improves patient health outcomes.

### Randomized Controlled Trials

No additional RCTs that were not included in the Shevoja (2023) publication described above were identified that evaluated the diagnostic accuracy of TBS for vertebral fractures risk were identified.

### Nonrandomized Studies

In 2017, Martineau examined the clinical utility of using lumbar spine TBS in altering patient treatment[27]. A total of 34,316 women were included, all of whom had observational measurements (DXA, FRAX, TBS) for a minimum of 5 years. Overall, researchers identified that when using TBS, less than 5% of patients were reclassified for fracture risk compared to the FRAX score. Of these 5%, >90% of patients were defined as close to the intervention threshold. Overall, these findings showed a small, but significant improvement in major osteoporotic fracture and hip fracture assessment when using the lumbar spine TBS. These findings indicate that TBS may better identify patients with a high fracture risk compared to FRAX. Further research is needed to identify if the reclassification of patients improves health outcomes.

In 2016, researchers examined the utility of TBS among older men with a high body mass index [28]. TBS is not considered valid for patients with a body mass index >37 kg/$m^2$, so the aim of the study was to examine if TBS varied by BMI and body composition among older men. Researchers also examined the association between TBS and lumbar spine volumetric BMD (LS-VBMD). A total of 3,479 patients were included who had a TBS from spine DXA scans. Researchers identified that the relationship between TBS and LS-VBMD was nonlinear even after adjusting for age, clinical site, and BMI, trunk lean mass, or trunk fat mass. The magnitude of effect relating TBS and LS-VBMD decreased with an increasing BMI. Overall, the clinical utility of using TBS to identify fracture risk among older men with a high BMI or high trunk lean mass may be limited.

A cohort study by Iki examined whether TBS predicted the risk of vertebral fractures among 655 women (15-79 years) [29]. Among eligible participants, 92 suffered vertebral fractures, and were found to have lower BMD and TBS scores compared to those without fractures. Researchers identified that combining TBS and BMD significantly improved risk prediction accuracy compared to using BMD alone. TBS was also found to be associated with higher risk of vertebral fracture over 10 years independent of BMD. These findings compared the outcomes of two measurements which both utilize a DXA scan to predict fracture risk. When DXA scan is available, the utilization of BMD and TBS may improve fracture risk assessment.

### Section Summary

Many studies utilize TBS as an outcome variable when assessing bone microarchitectural changes and fracture risk following treatment in a randomized controlled trial. At this time, there is a lack of well-designed clinical trials showing the impact of adding the TBS on patient management or patient-health outcomes. Additional prospective trials evaluating the use of TBS in place of or in addition to established fracture prediction tools should be used to evaluate long-term patient health outcomes.

## PRACTICE GUIDELINE SUMMARY

### THE BONE HEALTH AND OSTEOPOROSIS FOUNDATION

The Bone Health and Osteoporosis Foundation, formerly the National Osteoporosis Foundation, published an updated clinician's guide to the prevention and treatment of osteoporosis in 2022.[30] Per the guide, "a vertebral fracture in an adult ≥ 50 years is diagnostic of osteoporosis, even in the absence of a bone density diagnosis. Unfortunately, most vertebral fractures are subclinical or completely asymptomatic. As a result, they may go undiagnosed for many years. At the same time, a high proportion of women with asymptomatic vertebral fractures have BMD levels that would not warrant treatment based on bone mineral density (BMD) alone. The finding of a previously unrecognized vertebral fracture may change a patient's diagnostic classification, alter fracture risk calculations, and determine treatment decisions. Proactive investigation is required to detect these fractures so that further bone damage can be prevented."

Traditionally, conventional lateral thoracic/lumbar spine X-ray has been considered the gold standard for identification of vertebral fractures; however, the guide notes that "DXA-assisted VFA is emerging as an alternative to radiograph for its convenience, low cost, and minimal radiation exposure." The guide recommends that to "to detect subclinical vertebral fractures," clinicians should perform vertebral fracture imaging (X-ray or DXA VFA) in the following:

> Women aged ≥ 65 years if T-score is ≤ -1.0 at the femoral neck;
>
> Women ≥ 70 years and men ≥ 80 years if T-score is ≤ -1.0 at the lumbar spine, total hip, or femoral neck;
>
> Men aged 70 to 79 years if T-score is ≤ -1.5 at the lumbar spine, total hip, or femoral neck;
>
> Postmenopausal women and men ≥50 years with the following specific risk factors:
>
> - Fracture(s) during adulthood (any cause).
> - Historical height loss of ≥ 1.5 inches (defined as the difference between the current height and peak height).
> - Prospective height loss of ≥ 0.8 inches (defined as the difference between the current height and last documented height measurement).
> - Recent or ongoing long-term glucocorticoid treatment.
> - Diagnosis of hyperparathyroidism.

### INTERNATIONAL SOCIETY FOR CLINICAL DENSITOMETRY (ISCD)

In 2023, the ISCD issued updated recommendations for selecting patients for vertebral fracture assessment.[31]. Lateral spine imaging with either standard radiography or densitometric VFA is indicated for individuals with a T-score of less than -1.0 when at least one of the following factors are present:

- Women age >70 or men >80 years
- Historical height loss >4 cm (>1.5 inches)
- Self-reported but undocumented prior vertebral fracture
- Glucocorticoid therapy equivalent to >5mg of prednisone per day for >3 months.

In a second 2013 ISCD guideline, “Indications of DXA in women younger than 65 yr and men younger than 70 yr: the 2013 Official Positions,” DXA was recommended in those postmenopausal women younger than 65 yr and men 50-69 yr only in the presence of clinical risk factors for low bone mass, such as low body weight, prior fracture, high-risk medication use, or a disease or condition associated with bone loss.[32]

In 2023, the ISCD issued updated recommendations regarding the use of TBS in patients (add title). While TBS has been associated with fracture risk in certain populations, they recommend that “in routine clinical practice, monitoring and reporting TBS change is not recommended”.

## AMERICAN ASSOCIATION OF CLINICAL ENDOCRINOLOGISTS (AACE) AND AMERICAN COLLEGE OF ENDOCRINOLOGY (ACE)

The 2016 AACE/ACE Clinical Practice Guidelines for the Diagnosis and Treatment of Postmenopausal Osteoporosis[33] state:

> “Vertebral fracture is the most common osteoporotic fracture and indicates a high risk for future fractures, even when the T-score does not meet the threshold for osteoporosis. Prevalent fractures, therefore, may change an individual’s diagnostic classification, estimated risk of future fractures, and clinical management…. Lateral spine imaging with standard radiography or VFA with DXA is indicated when T-score is <-1.0 and1 or more of the following is present:
>
> - Women aged ≥70 years or men aged ≥80 years
> - Historical height loss >4 cm (>1.5 inches)
> - Self-reported but undocumented prior vertebral fracture
> - Glucocorticoid therapy equivalent to ≥5 mg prednisone or equivalent per day for ≥3 months

## NORTH AMERICAN MENOPAUSE SOCIETY

The 2010 position statement on management of osteoporosis does not include a recommendation for or against vertebral fracture assessment as part of the screening process.[34] The statement states that vertebral fracture must be confirmed by lateral spine radiographs or VFA visualization of fracture at the time of BMD testing.

## U.S. PREVENTIVE SERVICES TASK FORCE (USPSTF)

The U.S. Preventive Services Task Force (2018) updated its recommendations on screening for osteoporosis to prevent fractures. The recommendations included: "Most treatment guidelines recommend using BMD, as measured by central DXA, to define osteoporosis and the treatment threshold to prevent osteoporotic fractures." Peripheral DXA and quantitative ultrasound are also described as common bone measurement screening tests for osteoporosis. VFA was not specifically mentioned.[35]

## AMERICAN COLLEGE OF RADIOLOGY

As of 2016, the American College of Radiology (ACR) recommend VFA DXA in lieu of spine x-ray for suspected fracture of a vertebral body based on clinical history, height loss or treatment with steroids.[36] The ACR guidelines note that, “The utility of VFA is in the identification of patients who would otherwise not qualify for treatment under the guidelines of the NOF, which are based solely on BMD measurements.”

## SUMMARY

There is not enough research to show that using DXA and/or trabecular bone score to screen for vertebral fractures or fracture risk can improve health outcomes for anyone, including those who may have decreased bone mineral density (BMD). Because the impact of screening for vertebral fractures or fracture risk using DXA and/or TBS as a stand-alone procedure or in addition to standard BMD studies on health outcomes is not known, these procedures are considered investigational.

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## CODES

| Codes | Number | Description |
|---|---|---|
| CPT | 77085 | Dual-energy X-ray absorptiometry (DXA), bone density study, 1 or more sites; axial skeleton (e.g., hips, pelvis, spine); axial skeleton (e.g., hips, pelvis, spine), including vertebral fracture assessment |
| | 77086 | Vertebral fracture assessment via dual-energy X-ray absorptiometry (DXA) |
| | 77089 | Trabecular bone score (TBS), structural condition of the bone microarchitecture; using dual X-ray absorptiometry (DXA) or other imaging data on gray-scale variogram, calculation, with interpretation and report on fracture-risk |
| | 77090 | Trabecular bone score (TBS), structural condition of the bone microarchitecture; technical preparation and transmission of data for analysis to be performed elsewhere |
| | 77091 | Trabecular bone score (TBS), structural condition of the bone microarchitecture; technical calculation only |

| Codes | Number | Description |
|---|---|---|
| | 77092 | Trabecular bone score (TBS), structural condition of the bone microarchitecture; interpretation and report on fracture-risk only by other qualified health care professional |
| HCPCS | None | |

***Date of Origin:*** *December 2005*