Osteoporosis and Bone Mineral Density
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
1. NIH Consensus Development Panel on Osteoporosis Prevention, Diagnosis and Therapy. Osteoporosis Prevention, Diagnosis, and Therapy. *JAMA.* 2001;285(6):785-795.	Review/Other-Dx	13 member panel	To clarify the factors associated with prevention, diagnosis, and treatment of osteoporosis, and to present the most recent information available in these areas.	Though prevalent in white postmenopausal women, osteoporosis occurs in all populations and at all ages and has significant physical, psychosocial, and financial consequences. Risks for osteoporosis (reflected by low BMD) and for fracture overlap but are not identical. More attention should be paid to skeletal health in persons with conditions associated with secondary osteoporosis. Clinical risk factors have an important but poorly validated role in determining who should have BMD measurement, in assessing fracture risk, and in determining who should be treated. Adequate calcium and vitamin D intake is crucial to develop optimal peak bone mass and to preserve bone mass throughout life. Supplementation with these 2 nutrients may be necessary in persons not achieving recommended dietary intake. Gonadal steroids are important determinants of peak and lifetime bone mass in men, women, and children. Regular exercise, especially resistance and high-impact activities, contributes to development of high peak bone mass and may reduce risk of falls in older persons. Assessment of bone mass, identification of fracture risk, and determination of who should be treated are the optimal goals when evaluating patients for osteoporosis. Fracture prevention is the primary treatment goal for patients with osteoporosis. Several treatments have been shown to reduce the risk of osteoporotic fractures, including those that enhance bone mass and reduce the risk or consequences of falls. Adults with vertebral, rib, hip or distal forearm fractures should be evaluated for osteoporosis and given appropriate therapy.	4

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2. *U.S. Department of Health and Human Services. Bone Health and Osteoporosis: A Report of the Surgeon General.*: Rockville, MD: U.S. Department of Health and Human Services, Office of the Surgeon General; 2004.	Review/Other-Dx	N/A	A report on bone health and osteoporosis.	N/A	4
3. Englander F, Hodson TJ, Terregrossa RA. Economic dimensions of slip and fall injuries. *J Forensic Sci.* 1996;41(5):733-746.	Review/Other-Dx	N/A	To provide an update of annual economic costs imposed by fall injuries.	No results stated in abstract.	4
4. Damilakis J, Adams JE, Guglielmi G, Link TM. Radiation exposure in X-ray-based imaging techniques used in osteoporosis. *Eur Radiol.* 2010;20(11):2707-2714.	Review/Other-Dx	N/A	The article provides (a) a brief review of the current X-ray methods used for quantitative assessment of the skeleton, (b) data on the levels of radiation exposure associated with these methods and (c) information about radiation safety issues.	No results stated.	4
5. Cummings SR, Black DM, Nevitt MC, et al. Bone density at various sites for prediction of hip fractures. The Study of Osteoporotic Fractures Research Group. *Lancet.* 1993;341(8837):72-75.	Experimental-Dx	8,134 women	To determine the best measurement for predicting hip fractures, the authors assessed bone density of the hip, spine, radius, and calcaneus in a cohort of older women, and followed them for the occurrence of hip fractures.	65 women had hip fractures during a mean follow-up of 1.8 years. Each SD decrease in femoral neck bone density increased the age-adjusted risk of hip fracture 2.6 times (95% CL 1.9, 3.6). Women with bone density in the lowest quartile had an 8.5-fold greater risk of hip fracture than those in the highest quartile. Bone density of the femoral neck was a better predictor than measurements of the spine ($P<0.0001$), radius ($P<0.002$), and moderately better than the calcaneus ($P=0.10$). Low hip bone density is a stronger predictor of hip fracture than bone density at other sites. Efforts to prevent hip fractures should focus on women with low hip bone density.	3

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6. Hui SL, Slemenda CW, Johnston CC, Jr. Age and bone mass as predictors of fracture in a prospective study. *J Clin Invest.* 1988;81(6):1804-1809.	Review/Other-Dx	521 Caucasian women	To study the effect of bone mass on the risk of fracture.	The authors observed 138 nonspinal fractures in 3,388 person-years. The person-years of follow-up and the incident fractures were cross-classified by age and bone mass. The incidence of fracture was then fitted to a log-linear model in age and bone mass. It was found that incidence of fracture increased with both increasing age and decreasing radius bone mass. When subsets of fractures were examined it was found that age was a stronger predictor of hip fractures, whereas midshaft radius bone mass was a stronger predictor of fractures at the distal forearm. The authors concluded that bone mass is a useful predictor of fractures but that other age-related factors associated with fractures need to be identified.	4
7. Kanis JA, Borgstrom F, De Laet C, et al. Assessment of fracture risk. *Osteoporos Int.* 2005;16(6):581-589.	Review/Other-Dx	N/A	To review the assessment of fracture risk.	No results stated in abstract.	4
8. Kanis JA, Johnell O, De Laet C, et al. A meta-analysis of previous fracture and subsequent fracture risk. *Bone.* 2004;35(2):375-382.	Meta-analysis	15,259 men and 44,902 women	To quantify this risk on an international basis and to explore the relationship of this risk with age, sex, and BMD.	The results of the different studies were merged by using the weighted beta-coefficients. A previous fracture history was associated with a significantly increased risk of any fracture compared with individuals without a prior fracture (RR = 1.86; 95% CI = 1.75–1.98). The RR was similar for the outcome of osteoporotic fracture or for hip fracture. There was no significant difference in RR between men and women. RR was marginally downward adjusted when account was taken of BMD. Low BMD explained a minority of the risk for any fracture (8%) and for hip fracture (22%). The RR was stable with age except in the case of hip fracture outcome where the RR decreased significantly with age.	M

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
9. Kanis JA, Johnell O, Oden A, Dawson A, De Laet C, Jonsson B. Ten year probabilities of osteoporotic fractures according to BMD and diagnostic thresholds. *Osteoporos Int.* 2001;12(12):989-995.	Review/Other-Dx	N/A	To estimate 10 year probabilities of osteoporotic fractures in men and women according to age and BMD at the femoral neck.	The 10-year probability of any fracture was determined from the proportion of individuals fracture-free from the age of 45 years. With the exception of forearm fractures in men, 10 year probabilities increased with age and T-score. In the case of hip and spine fractures, fracture probabilities for any age with low BMD were similar between men and women. The effect of age on risk independently of BMD suggests that intervention thresholds should not be at a fixed T-score but vary according to absolute probabilities. Intervention thresholds based on hip BMD T-scores are similar between sexes.	4
10. Brown JP, Josse RG. 2002 clinical practice guidelines for the diagnosis and management of osteoporosis in Canada. *CMAJ.* 2002;167(10 Suppl):S1-34.	Review/Other-Dx	N/A	To revise and expand the 1996 Osteoporosis Society of Canada clinical practice guidelines for the management of osteoporosis, incorporating recent advances in diagnosis, prevention and management of osteoporosis, and to identify and assess the evidence supporting the recommendation.	N/A	4
11. Hansen MA, Hassager C, Overgaard K, Marslew U, Riis BJ, Christiansen C. Dual-energy x-ray absorptiometry: a precise method of measuring bone mineral density in the lumbar spine. *J Nucl Med.* 1990;31(7):1156-1162.	Review/Other-Dx	forearm was measured	To compare two methods of measuring spinal bone mineral content and BMD: conventional dual-photon absorptiometry and a more recent method, DXA.	DXA had a long-term in vivo precision of 1% which was significantly better than that of dual-photon absorptiometry. Changes in the distribution of fatty tissue influenced the accuracy of the 2 spinal methods in different ways. Forearm bone mineral content discriminated between the bone mass of early and late postmenopausal women to the same degree as dual-photon absorptiometry and DXA. The variability in the response to estrogen treatment and placebo was much lower with DXA and forearm bone mineral content than with dual-photon absorptiometry. The authors conclude that DXA provides a fast and precise measurement of spinal bone mineral content/BMD. The accuracy remains to be evaluated for in vivo studies.	4

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12. Shepherd JA, Schousboe JT, Broy SB, Engelke K, Leslie WD. Executive Summary of the 2015 ISCD Position Development Conference on Advanced Measures From DXA and QCT: Fracture Prediction Beyond BMD. *J Clin Densitom.* 2015;18(3):274-286.	Review/Other-Dx	N/A	To describe the methodology of the 2015 ISCD Position Development Conference and the results from the topics regarding advanced measures from DXA and QCT for fracture prediction beyond BMD.	N/A	4
13. Kanis JA. Diagnosis of osteoporosis and assessment of fracture risk. *Lancet.* 2002;359(9321):1929-1936.	Review/Other-Dx	N/A	To review diagnosis of osteoporosis and assessment of fracture risk.	The diagnosis of osteoporosis is generally based on assessment of BMD at the proximal femur by DXA. By contrast, intervention thresholds should be based on fracture probability. Several clinical risk factors for fracture with and without BMD allow the more accurate stratification of risk than the use of BMD alone. In the absence of validated screening strategies, a case-finding approach is advocated for individuals with strong risk factors who are referred for BMD assessment. Intervention is best targeted to those in whom fracture probability exceeds a threshold of reversible risk, based on cost-effectiveness.	4
14. Genant HK, Cooper C, Poor G, et al. Interim report and recommendations of the World Health Organization Task-Force for Osteoporosis. *Osteoporos Int.* 1999;10(4):259-264.	Review/Other-Dx	N/A	Interim report and recommendations of the World Health Organization Task-Force for osteoporosis.	N/A	4
15. Kanis JA, McCloskey EV, Johansson H, Oden A, Strom O, Borgstrom F. Development and use of FRAX in osteoporosis. *Osteoporos Int.* 2010;21 Suppl 2:S407-413.	Review/Other-Dx	N/A	To review briefly the development and clinical use of FRAX in the development of assessment guidelines for osteoporosis.	The FRAX tool integrates information on fracture risk from clinical risk factors with or without the use of BMD and can be used to improve the targeting of individuals at high fracture risk.	4

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
16. Kanis JA, Hans D, Cooper C, et al. Interpretation and use of FRAX in clinical practice. *Osteoporos Int.* 2011;22(9):2395-2411.	Review/Other-Dx	N/A	The introduction of the WHO FRAX(R) algorithms has facilitated the assessment of fracture risk on the basis of fracture probability. Its use in fracture risk prediction has strengths, but also limitations of which the clinician should be aware and are the focus of this review.	Details on the clinical risk factors currently used in FRAX are provided, and the reasons for the exclusion of others are provided. Recommendations are made for the development of surrogate models where country-specific FRAX models are not available. The wish list of clinicians for the modulation of FRAX is large, but in many instances, these wishes cannot presently be fulfilled; however, an explanation and understanding of the reasons may be helpful in translating the information provided by FRAX into clinical practice.	4
17. Bilezikian JP, Khan AA, Potts JT, Jr. Guidelines for the management of asymptomatic primary hyperparathyroidism: summary statement from the third international workshop. *J Clin Endocrinol Metab.* 2009;94(2):335-339.	Review/Other-Dx	N/A	Guidelines for the management of asymptomatic PHPT.	N/A	4
18. American College of Radiology. ACR–SPR–SSR Practice Parameter for the Performance of Dual-Energy X-Ray Absorptiometry (DXA) . Available at: http://www.acr.org/~/media/ACR/Documents/PGTS/guidelines/DXA.pdf. 2014.	Review/Other-Dx	N/A	Guidance document to promote the safe and effective use of diagnostic and therapeutic radiology by describing specific training, skills and techniques.	N/A	4
19. American College of Radiology. ACR–SPR–SSR Practice Parameter for the Performance of Quantitative Computed Tomography (QCT) Bone Densitometry. Available at: http://www.acr.org/~/media/ACR/Documents/PGTS/guidelines/QCT.pdf. 2014.	Review/Other-Dx	N/A	Guidance document to promote the safe and effective use of diagnostic and therapeutic radiology by describing specific training, skills and techniques.	N/A	4
20. Edelstyn GA, Gillespie PJ, Grebbell FS. The radiological demonstration of osseous metastases. Experimental observations. *Clin Radiol.* 1967;18(2):158-162.	Review/Other-Dx	N/A	To examine the efficiency of conventional radiological methods in detecting osseous destruction.	Using human lumbar vertebrae, detection of a defect on lateral x-ray was only possible when between 50 9/00 and 75 ~ of the cancellous bone thickness had been removed, whilst on A.P. view a greater deficit was necessary.	4
21. Durosier C, Hans D, Krieg MA, Schott AM. Prediction and discrimination of osteoporotic hip fracture in postmenopausal women. *J Clin Densitom.* 2006;9(4):475-495.	Review/Other-Dx	N/A	A review based on original articles and meta-analyses to predict the risk of hip fracture and to discriminate individuals with or without fracture.	No results stated.	4

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
22. Krieg MA, Barkmann R, Gonnelli S, et al. Quantitative ultrasound in the management of osteoporosis: the 2007 ISCD Official Positions. *J Clin Densitom.* 2008;11(1):163-187.	Review/Other-Dx	N/A	The ISCD 2007 PDC addressed clinical applications of QUS for fracture risk assessment, diagnosis of osteoporosis, treatment initiation, monitoring of treatment, and quality assurance/quality control. The ISCD Official Positions on QUS resulting from this PDC, the rationale for their establishment, and recommendations for further study are presented in the document.	N/A	4
23. Marin F, Gonzalez-Macias J, Diez-Perez A, Palma S, Delgado-Rodriguez M. Relationship between bone quantitative ultrasound and fractures: a meta-analysis. *J Bone Miner Res.* 2006;21(7):1126-1135.	Meta-analysis	47,300 individuals and 2,350 incident fractures	To determine the association between measurements of QUS with the risk of fracture.	11 studies evaluated QUS at the heel, with patella and phalanx (2 studies each) and distal radius (1 study) being scarcely used. There was not significant heterogeneity among the studies included in the review. Relative risk estimates (95% CI) for overall fractures were 1.55 (1.35–1.78) for each SD decrease in broadband US attenuation, 1.63 (1.37–1.93) for speed of sound, and 1.74 (1.39–2.17) for QUS index/stiffness index. Risk estimates were similar or slightly higher for hip fractures and low-energy trauma fractures. Humeral and forearm/wrist fractures were also related with lower QUS values.	M
24. Marshall D, Johnell O, Wedel H. Meta-analysis of how well measures of bone mineral density predict occurrence of osteoporotic fractures. *Bmj.* 1996;312(7041):1254-1259.	Meta-analysis	11 separate study populations with about 90,000 person years of observation time and over 2,000 fractures	To determine the ability of measurements of bone density in women to predict later fractures.	All measuring sites had similar predictive abilities (relative risk 1.5 (95% CI, 1.4 to 1.6)) for decrease in BMD except for measurement at spine for predicting VFs (relative risk 2.3 (1.9 to 2.8)) and measurement at hip for hip fractures (2.6 (2.0 to 3.5)). These results are in accordance with results of case-control studies. Predictive ability of decrease in bone mass was roughly similar to (or, for hip or spine measurements, better than) that of a 1 SD increase in blood pressure for stroke and better than a 1 SD increase in serum cholesterol concentration for cardiovascular disease.	M

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25. Forsen L, Berntsen GK, Meyer HE, Tell GS, Fonnebo V. Differences in precision in bone mineral density measured by SXA and DXA: the NOREPOS study. *Eur J Epidemiol.* 2008;23(9):615-624.	Review/Other-Dx	207 participants	To compare the precision (reliability) in single X-ray and DXA, and to compare smallest detectable difference.	The precision was estimated by Root Mean Square Standard Deviation (RMS SD) with 95% CI and the corresponding coefficients of variation. Determinants (age, gender, BMD) were analyzed by multiple linear regression with log (SD) and log (coefficients of variation) as dependent variables. RMS SD tended to be largest in older women and in those with low BMD. RMS SD for single X-ray and DXA forearm was 4.6 (4.2–5.1) and 6.8 (6.1–7.4) and the corresponding CVs 1.0% and 1.4%. RMS SD for DXA hip was 11.0 (9.9–12.0) with coefficients of variation 1.2%.	4
26. Engelke K, Adams JE, Armbrecht G, et al. Clinical use of quantitative computed tomography and peripheral quantitative computed tomography in the management of osteoporosis in adults: the 2007 ISCD Official Positions. *J Clin Densitom.* 2008;11(1):123-162.	Review/Other-Dx	N/A	To present the ISCD Official Positions for QCT and pQCT, with supporting medical evidence, rationale, controversy, and suggestions for further study.	N/A	4
27. Lochmuller EM, Muller R, Kuhn V, Lill CA, Eckstein F. Can novel clinical densitometric techniques replace or improve DXA in predicting bone strength in osteoporosis at the hip and other skeletal sites? *J Bone Miner Res.* 2003;18(5):906-912.	Review/Other-Dx	126 human cadavers	To test the hypothesis that pQCT at the distal radius and/or QUS at the calcaneus can serve as replacement or improvement of current methodology (QCT and DXA) for predicting bone strength at the hip and other sites.	Site-specific DXA explained approximately 55% of the variability in femoral strength, whereas pQCT and QUS displayed a lower association (15%–40%). QUS did not provide additional information on mechanical strength of the femur, spine, or radius. All techniques displayed similar capability in predicting a combined index of failure strength at these 3 sites, with only QUS exhibiting significantly lower associations than other methods. These experimental results suggest that clinical assessment of femoral fracture risk should preferably rely on femoral DXA, whereas DXA, QCT, and pQCT display similar capability of predicting a combined index of mechanical strength at the hip, spine, and radius.	4

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
28. Silva BC, Leslie WD, Resch H, et al. Trabecular bone score: a noninvasive analytical method based upon the DXA image. *J Bone Miner Res.* 2014;29(3):518-530.	Review/Other-Dx	N/A	A review on TBS.	The following conclusions are based upon publications reviewed in this article: 1) TBS gives lower values in postmenopausal women and in men with previous fragility fractures than their nonfractured counterparts; 2) TBS is complementary to data available by lumbar spine DXA measurements; 3) TBS results are lower in women who have sustained a fragility fracture but in whom DXA does not indicate osteoporosis or even osteopenia; 4) TBS predicts fracture risk as well as LS-BMD measurements in postmenopausal women; 5) efficacious therapies for osteoporosis differ in the extent to which they influence the TBS; 6) TBS is associated with fracture risk in individuals with conditions related to reduced bone mass or bone quality. Based on these data, lumbar spine TBS holds promise as an emerging technology that could well become a valuable clinical tool in the diagnosis of osteoporosis and in fracture risk assessment.	4
29. Del Rio LM, Winzenrieth R, Cormier C, Di Gregorio S. Is bone microarchitecture status of the lumbar spine assessed by TBS related to femoral neck fracture? A Spanish case-control study. *Osteoporos Int.* 2013;24(3):991-998.	Review/Other-Dx	191 Spanish women: 83 subjects with a fracture and 108 control subjects	To evaluate the ability of TBS at lumbar spine to discriminate subjects with hip fracture.	The study population consisted of 83 subjects with a fracture and 108 control subjects. Significant lower spine and hip BMD and TBS values were found for subjects with fractures ($P<0.0001$). Correlation between LS-BMD and spine TBS was modest (r = 0.41, $P<0.05$). LS-BMD and TBS independently discriminate fractures equally well (OR = 2.21 [1.56–3.13] and 2.05 [1.45–2.89], respectively) but remain lower than BMD at neck or at total femur (OR = 5.86 [3.39–10.14] and 6.06 [3.55–10.34], respectively). After adjusting for age, LS-BMD and TBS remain significant for transcervical fracture discrimination (OR = 1.94 [1.35–2.79] and 1.71 [1.15–2.55], respectively). TBS and LS-BMD combination (OR = 2.39 [1.70–3.37]) improved fracture risk prediction by 25%.	4

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30. Krueger D, Fidler E, Libber J, Aubry-Rozier B, Hans D, Binkley N. Spine trabecular bone score subsequent to bone mineral density improves fracture discrimination in women. *J Clin Densitom.* 2014;17(1):60-65.	Observational-Dx	158 women with fracture and 271 age-matched controls	To evaluate the ability of TBS measurement to discriminate between older women with prior fragility fracture, including unappreciated VF, from those without fracture, independent of their BMD. Additionally, the authors investigated whether the combination of TBS and BMD enhances fracture detection compared with either measurement alone.	The correlation between LS-BMD and TBS was low (r = 0.28), suggesting these parameters reflect different bone properties. Age- and BMI-adjusted ORs ranged from 1.36 to 1.63 for LS or hip BMD in discriminating women with low trauma nonvertebral and VFs. TBS demonstrated ORs from 2.46 to 2.49 for these respective fractures; these remained significant after lowest BMD T-score adjustment (OR = 2.38 and 2.44). 73% of all fractures occurred in women without osteoporosis (BMD T-score > -2.5); 72% of these women had a TBS score below the median, thereby appropriately classified them as being at increased risk. In conclusion, TBS assessment enhances DXA by evaluating trabecular pattern and identifying individuals with vertebral or low trauma fracture. TBS identifies 66%–70% of women with fracture who were not classified with osteoporosis by BMD alone.	3
31. Lamy O, Krieg MA, Stoll D, Aubry-Rozier B, Metzger M, Hans D. The OsteoLaus Cohort Study. Bone mineral density, micro-architecture score and vertebral fracture assessment extracted from a single DXA device in combination with clinical risk factors improve significantly the identification of women at high risk of fracture. *Osteologie.* 2012;21(2):77-82.	Review/Other-Dx	631 women	To combine Clinical Risk Factor and the information given by DXA BMD, TBS and VFA to better identify women at high fracture risk.	Prevalence of VFs grade 2/3, major osteoporosis fracture and all osteoporosis fracture was 8.4%, 17.0% and 26.0%, respectively. Age- and BMI-adjusted ORs (per SD decrease) were 1.8 (1.2–2.5), 1.6 (1.2–2.1), 1.3 (1.1–1.6) for BMD and 2.0 (1.4–3.0), 1.9 (1.4–2.5), 1.4 (1.1–1.7) for TBS respectively. The TBS ORs (per SD decrease) adjusted for age, BMI and spine BMD for VFs grade 2/3, major and all osteoporosis fracture were 1.7 (1.1–2.7),1.6 (1.2–2.2) and 1.3 (1.0–1.7) respectively. Only 35% to 44 % of women with osteoporosis fracture had a BMD < –2.5 SD or a TBS < 1.200. If authors combine a BMD < –2.5 SD or a TBS < 1.200, 54 to 60 % of women with an osteoporosis fracture are identified.	4

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32. Pothuaud L, Barthe N, Krieg MA, Mehsen N, Carceller P, Hans D. Evaluation of the potential use of trabecular bone score to complement bone mineral density in the diagnosis of osteoporosis: a preliminary spine BMD-matched, case-control study. *J Clin Densitom.* 2009;12(2):170-176.	Observational-Dx	45 women with osteoporotic fractures (5 hip fractures, 20 VFs, and 20 other types of fracture) and 155 women without a fracture	A preliminary case-control study to evaluate the potential diagnostic value of TBS as a complement to BMD, by comparing postmenopausal women with and without fractures.	TBS measured at the total spine revealed a significant difference between the fracture and age- and spine BMD-matched nonfracture group, when considering all types of fractures and VFs. In these cases, the diagnostic value of the combination of BMD and TBS likely will be higher compared with that of BMD alone. TBS, as evaluated from standard DXA scans directly, potentially complements BMD in the detection of osteoporotic fractures.	3
33. Rabier B, Heraud A, Grand-Lenoir C, Winzenrieth R, Hans D. A multicentre, retrospective case-control study assessing the role of trabecular bone score (TBS) in menopausal Caucasian women with low areal bone mineral density (BMDa): Analysing the odds of vertebral fracture. *Bone.* 2010;46(1):176-181.	Observational-Dx	42 women with osteoporosis-related VFs and 126 age-matched women without any fractures	Case-control study to evaluate the potential diagnostic value of TBS, both alone and combined with areal BMD, in the assessment of VF.	Across all subjects (n=42,126) weight and BMI were greater and areal BMD and TBS both less in women with fractures. The odds of VF were 3.20 (95% CI, 2.01–5.08) for each incremental decrease in TBS, 1.95 (1.34–2.84) for areal BMD, and 3.62 (2.32–5.65) for areal BMD + TBS combined. The AUC was greater for TBS than for areal BMD (0.746 vs 0.662, *P*=0.011). At iso-specificity (61.9%) or iso-sensitivity (61.9%) for both areal BMD and TBS, TBS + areal BMD sensitivity or specificity was 19.1% or 16.7% greater than for either areal BMD or TBS alone. Among subjects with osteoporosis (n=11, 40) both areal BMD (*P*=0.0008) and TBS (*P*=0.0001) were lower in subjects with fractures, and both OR and AUC (*P*=0.013) for areal BMD + TBS were greater than for areal BMD alone (OR=4.04 [2.35–6.92] vs 2.43 [1.49–3.95]; AUC=0.835 [0.755–0.897] vs 0.718 [0.627–0.797], *P*=0.013). Among subjects with osteopenia, TBS was lower in women with fractures (*P*=0.0296), but areal BMD was not (*P*=0.75). Similarly, the OR for TBS was statistically >1.00 (2.82, 1.27–6.26), but not for areal BMD (1.12, 0.56–2.22), as was the AUC (*P*=0.035), but there was no statistical difference in specificity (*P*=0.357) or sensitivity (*P*=0.678).	3

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34. Silva BC, Boutroy S, Zhang C, et al. Trabecular bone score (TBS)--a novel method to evaluate bone microarchitectural texture in patients with primary hyperparathyroidism. *J Clin Endocrinol Metab.* 2013;98(5):1963-1970.	Review/Other-Dx	22 postmenopausal women with PHPT	To assess TBS from spine DXA images in relation to HR-pQCT indices and bone stiffness in radius and tibia in PHPT.	TBS in PHPT was low at 1.24, representing abnormal trabecular microstructure (normal ≥1.35). TBS was correlated with whole bone stiffness and all HR-pQCT indices, except for trabecular thickness and trabecular stiffness at the radius. At the tibia, correlations were observed between TBS and volumetric densities, cortical thickness, trabecular bone volume, and whole bone stiffness. TBS correlated with all indices of trabecular microarchitecture, except trabecular thickness, after adjustment for body weight.	4
35. Winzenrieth R, Dufour R, Pothuaud L, Hans D. A retrospective case-control study assessing the role of trabecular bone score in postmenopausal Caucasian women with osteopenia: analyzing the odds of vertebral fracture. *Calcif Tissue Int.* 2010;86(2):104-109.	Observational-Dx	81 women with osteoporosis-related VFs and 162 age-matched controls without fractures	To assess whether the TBS, determined from gray-level analysis of DXA images, might be of any diagnostic value, either alone or combined with BMD, in the assessment of VF risk among postmenopausal women with osteopenia.	Primary outcomes were BMD and TBS. For BMD, each incremental decrease in BMD was associated with an OR = 1.54 (95% CI = 1.17–2.03), and the AUC was 0.614 (0.550–0.676). For TBS, corresponding values were 2.53 (1.82–3.53) and 0.721 (0.660–0.777). The difference in the AUC for TBS vs BMD was statistically significant (P=0.020). The OR for (TBS + BMD) was 2.54 (1.86–3.47) and the AUC 0.732 (0.672–0.787). In conclusion, the TBS warrants a closer look to see whether it may be of clinical usefulness in the determination of fracture risk in postmenopausal osteopenic women.	3
36. Leslie W, Kanis JA, Lamy O, Johansson H, McCloskey EV, Hans D. Adjustment of FRAX probability according to lumbar spine Trabecular Bone Score (TBS): The Manitoba BMD Cohort. *Journal of Clinical Densitometry.* 2013;16(3):267-268.	Review/Other-Dx	42,170 women	The authors assessed the value of combining FRAX probability with lumbar spine TBS.	During mean 5.6 years, incident major osteoporotic fractures were identified in 2,661 women (674 hip fractures). Lower lumbar spine TBS and higher FRAX probabilities were found in fracture vs nonfracture women (all P<0.001). TBS modulated fracture risk after adjustment for treatment and individual FRAX risk factors (HR per SD reduction in TBS: major osteoporotic fracture 1.21 [95% CI, 1.16–1.250, P<0.001; hip fracture 1.14 [95% CI, 1.05–1.23), P=0.001). An incremental improvement in fracture prediction was seen by using lumbar spine TBS in combination with FRAX.	4

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
37. Eller-Vainicher C, Filopanti M, Palmieri S, et al. Bone quality, as measured by trabecular bone score, in patients with primary hyperparathyroidism. *Eur J Endocrinol.* 2013;169(2):155-162.	Observational-Dx	74 postmenopausal females and 18 eugonadal males	To evaluate the usefulness of TBS alone or in combination with BMD for predicting VF in PHPT patients before and after surgery or a conservative follow-up.	PHPT patients had lower TBS (-2.39+/-1.8) and higher VF prevalence (43.5%) than controls (-0.98+/-1.07 and 8.2% respectively, both $P<0.0001$). TBS was associated with VF (OR 1.4, 95% CI, 1.1–1.9, $P=0.02$), regardless of LS-BMD, age, BMI and gender, and showed a better compromise between sensitivity (75%) and specificity (61.5%) for detecting VF than LS-BMD, total hip-BMD and femoral neck-BMD (31% and 75%, 72% and 44.2%, and 64% and 65% respectively). In surgically treated patients, TBS, LS-BMD, total hip-BMD and femoral neck-BMD increased (+47+/-44.8,+29.2+/-34.1,+49.4+/-48.7 and +30.2+/-39.3% respectively, all $P<0.0001$). Among patients treated conservatively, TBS decreased significantly in those (n=3) with incident VF (-1.3+/-0.3) compared with those without (-0.01+/-0.9, $P=0.048$), while BMD changes were not statistically different (LS 0.3+/-1.2 vs -0.8+/-0.9 respectively, P=0.19; total hip 0.4+/-0.8 vs -0.8+/-1.4 respectively, P=0.13 and femoral neck 0.4+/-0.9 vs -0.8+/-1.4 respectively, $P=0.14$).	2

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
38. Leslie WD, Aubry-Rozier B, Lamy O, Hans D. TBS (trabecular bone score) and diabetes-related fracture risk. *J Clin Endocrinol Metab.* 2013;98(2):602-609.	Observational-Dx	29,407 women	To evaluate the ability of lumbar spine TBS to account for increased fracture risk in diabetes.	Diabetes was associated with higher BMD at all sites but lower lumbar spine TBS in unadjusted and adjusted models (all $P<.001$). The adjusted OR for a measurement in the lowest vs the highest tertile was <1 for BMD (all $P<.001$) but was increased for lumbar spine TBS [adjusted OR 2.61, 95% CI, 2.30–2.97]. Major osteoporotic fractures were identified in 175 women (7.4%) with and 1,493 (5.5%) without diabetes ($P<.001$). Lumbar spine TBS was a BMD-independent predictor of fracture and predicted fractures in those with diabetes (adjusted HR 1.27, 95% CI, 1.10–1.46) and without diabetes (HR 1.31, 95% CI, 1.24–1.38). The effect of diabetes on fracture was reduced when lumbar spine TBS was added to a prediction model but was paradoxically increased from adding BMD measurements.	4

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
39. Romagnoli E, Cipriani C, Nofroni I, et al. "Trabecular Bone Score" (TBS): an indirect measure of bone micro-architecture in postmenopausal patients with primary hyperparathyroidism. *Bone.* 2013;53(1):154-159.	Observational-Dx	73 postmenopausal women with PHPT and 74 age-matched healthy women	To investigate TBS in patients with PHPT.	Mean TBS values were significantly reduced in PHPT (1.19 +/- 0.10) compared to control (1.24 +/- 0.09, *P*<0.01). Patients and controls did not differ for age, years since menopause, BMI, 25(OH)D serum levels, creatinine clearance, LS-BMD and femoral neck-BMD. On the contrary, mean BMD values at both total hip and radius were significantly lower in PHPT patients compared to controls (*P*<0.01 and *P*<0.0001, respectively). In PHPT with VFs (n=29) TBS was significantly lower than in those without fracture (n=44) (1.14 +/- 0.10 vs 1.22 +/- 0.10, respectively; *P*<0.01), whose TBS values did not differ from controls. Mean TBS values in patients with (n=18) and without (n=55) nonVFs did not significantly differ (1.16 +/- 0.09 vs 1.20 +/- 0.11). The presence of VFs was independently associated with the reduction of TBS (OR=0.003, 95% CI=0-0.534, *P* =0.028) and with years since menopause (OR=1.076, 95% CI=1.017-1.139, *P* =0.011), but not with age, the reduction of LS-BMD and the increase of BMI. The combination of years since menopause >10 years plus TBS <1.2 was associated with a significant risk of VF (OR=11.73, 95% CI, 2.43–66.55, *P*<0.001). A TBS value <1.2 showed a better performance in individuating VF (sensibility 79.3%, specificity 61.4%, positive predictive value 57.5%, and negative predictive value 81.8%) in respect to years since menopause >10 years.	3

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
40. Black DM, Arden NK, Palermo L, Pearson J, Cummings SR. Prevalent vertebral deformities predict hip fractures and new vertebral deformities but not wrist fractures. Study of Osteoporotic Fractures Research Group. *J Bone Miner Res.* 1999;14(5):821-828.	Review/Other-Dx	9,704 women	To examine the association between prevalent vertebral deformities and incident osteoporotic fractures in the Study of Osteoporotic Fractures.	During follow-up, 389 women with new vertebral deformities, 464 with hip fractures, and 574 with wrist fractures were identified. Prevalent vertebral deformities were associated with a 5-fold increased risk (relative risk 5.4, 95% CI, 4.4, 6.6) of sustaining a further vertebral deformity; the risk increased dramatically with both the number and severity of the prevalent deformities. Similarly, the risks of hip and any nonVFs were increased with baseline prevalent deformity, with relative risks of 2.8 (95% CI, 2.3, 3.4) and 1.9 (95% CI, 1.7, 2.1), respectively. Risk increased with number and severity of deformities. These associations remained significant after adjustment for age and calcaneal BMD. Although there was a small increased risk of wrist fracture, this was not significant after adjusting for age and BMD.	4
41. Rosen HN, Vokes TJ, Malabanan AO, et al. The Official Positions of the International Society for Clinical Densitometry: vertebral fracture assessment. *J Clin Densitom.* 2013;16(4):482-488.	Review/Other-Dx	N/A	The 2007 PDC developed detailed guidelines regarding the indications for acquisition of, and interpretation and reporting of densitometric VFA tests. The purpose of the 2013 VFA Task Force was to simplify the indications for VFA yet keep them evidence based.	N/A	4
42. Genant HK, Wu CY, van Kuijk C, Nevitt MC. Vertebral fracture assessment using a semiquantitative technique. *J Bone Miner Res.* 1993;8(9):1137-1148.	Review/Other-Dx	57 postmenopausal women	To determine the incidence and prevalence of VFs postmenopausal women (age 65–75 years) by 3 independent observers.	The results show excellent intraobserver agreement and good interobserver agreement for the semiquantitative technique. The authors conclude that the semiquantitative approach can be applied reliably in VFA when performed using well-defined criteria.	4

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
43. Siris ES, Genant HK, Laster AJ, Chen P, Misurski DA, Krege JH. Enhanced prediction of fracture risk combining vertebral fracture status and BMD. *Osteoporos Int.* 2007;18(6):761-770.	Review/Other-Dx	2,651 postmenopausal women	To quantify the impact of VF burden on 2 year fracture risk across a range of BMD T-scores.	Femoral neck BMD T-score provided significant information regarding fracture risk. Across the range of T-scores, VF status provided additional prognostic information. The risk increased with increasing number and severity of prevalent VFs and spinal deformity index, a summary measure of spine fracture burden. Across a range of BMD values, prevalent spine fracture burden as assessed by spinal deformity index increased the risk of incident VFs by up to 12-fold, nonVFs by about twofold, and any fractures by up to sevenfold.	4
44. Jager PL, Jonkman S, Koolhaas W, Stiekema A, Wolffenbuttel BH, Slart RH. Combined vertebral fracture assessment and bone mineral density measurement: a new standard in the diagnosis of osteoporosis in academic populations. *Osteoporos Int.* 2011;22(4):1059-1068.	Review/Other-Dx	2,500 patients	To prospectively study VFA, which was applied routinely in all patients referred for BDM measurement to assess the rate of VF and used questionnaires to study the impact on management.	In 2,424 patients (1,573 women), results were evaluable. In 541 patients (22%), VFA detected a prevalent VF that was unknown in 69%. In women, the prevalence was 20% vs 27% found in men ($P<0.0001$). The prevalence of VF was 14% in patients with normal BMD (97/678), increased to 21% (229/1,100) in osteopenia and to 26% in those with osteoporosis (215/646) by WHO criteria. After excluding mild fractures, VF prevalence was 13% (322/2,424). In 468/942 questionnaires (50% response rate), 27% of the referring physicians reported VFA results to impact on patient management.	4
45. Kanterewicz E, Puigoriol E, Garcia-Barrionuevo J, del Rio L, Casellas M, Peris P. Prevalence of vertebral fractures and minor vertebral deformities evaluated by DXA-assisted vertebral fracture assessment (VFA) in a population-based study of postmenopausal women: the FRODOS study. *Osteoporos Int.* 2014;25(5):1455-1464.	Review/Other-Dx	2,968 postmenopausal women	To assess the prevalence of VF and minor deformities in 2,968 postmenopausal women aged 59–70 years from a population-based cohort.	The prevalence of VF was 4.3%, and 17% of the participants had minor vertebral deformities. Low BMD was frequently observed in women with VF, with 4%, and 42% of participants showing osteoporosis and osteopenia. Minor vertebral deformities were observed in nearly 40% of women with VF. Multivariate logistic regression analysis showed that age, history of previous fracture, osteoporotic BMD, receiving anti-osteoporotic treatment, and current use of glucocorticoids were significantly associated with VF.	4

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
46. Mrgan M, Mohammed A, Gram J. Combined vertebral assessment and bone densitometry increases the prevalence and severity of osteoporosis in patients referred to DXA scanning. *J Clin Densitom.* 2013;16(4):549-553.	Review/Other-Dx	3,275 patients	To assess if VFA after routine BMD measurement on a DXA machine had increased the number of patients diagnosed with osteoporosis and revealed previous unknown incident VFs.	Among the 3,275 patients, 85% were females and 15% were males. In total, 68% of the patients had normal BMD, and 32% had osteoporosis. VFs diagnosed by VFA were seen in 7.9% patients, of which 3.2% had normal BMD and 4.8% had osteoporosis assessed by BMD. The relative number of patients diagnosed with osteoporosis increased 9.79% and in absolute terms from 32.4% to 35.6% of patients referred to DXA. Addition of VFA to routine BMD measurement increased clinically significant the number of patients diagnosed with osteoporosis as well as the number of patients with fractures and thereby altered the severity and prognosis.	4
47. Greenblatt D, Jones LA, Wilson KE. Use of instant vertebral assessment in an internal medicine practice. *J Bone Miner Res.* 2002;17:S640.	Review/Other-Dx	172 patients	To examine the prevalence of VFs with respect to age and BMD status in patients referred for osteoporosis evaluation from within a multi-specialty internal medicine group.	In this study population, the presence of Normal or osteopenic BMD did not rule out the possibility of a prevalent VF. 20% of the women in the age range of 60–69 and >40% of the women over the age of 70 had a prevalent VF.	4
48. Nattrass SM, Jones LA, Kelly TL, von Stetten E, Wilson KE. Vertebral fractures identified by IVA in postmenopausal women. *J Bone Miner Res.* 2001;16(S1):S515.	Review/Other-Dx	158 postmenopausal women	The study identified prevalent VFs using the Instant Vertebral Assessment feature of the Hologic Delphi bone densitometer in postmenopausal women who came for BMD measurements to the Osteoporosis Research Unit at PacMed Clinics in Seattle, WA.	20% of the patients who were classified as normal or osteopenic by the BMD T-score had a VF. The use of the Instant Vertebral Assessment feature on these patients prevented them from being misclassified by BMD alone as low to moderate risk patients.	4
49. Vokes TJ, Dixon LB, Favus MJ. Clinical utility of dual-energy vertebral assessment (DVA). *Osteoporos Int.* 2003;14(11):871-878.	Observational-Dx	297 subjects (272 women)	To evaluate the clinical utility of dual-energy vertebral assessment, a system for imaging the lateral spine on the Lunar Prodigy densitometer.	Compared to radiographs, dual-energy vertebral assessment had a 95% sensitivity to detect fractures and 82% specificity (to exclude them). Among all 297 subjects studied, dual-energy vertebral assessments were interpretable in 87%. They were classified as N in 204 (68%), F in 55 (19%) and U in 38 (13%). The reasons for un-interpretability were: scoliosis, scapular or rib shadow, severe arthritic changes and multiple vertebral compression fracture with severe spinal deformities. Only 11% of F subjects gave a history of a VF, and only 56% of F subjects met the BMD criteria for osteoporosis (T score <-2.5).	2

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
50. Chesnut IC, Skag A, Christiansen C, et al. Effects of oral ibandronate administered daily or intermittently on fracture risk in postmenopausal osteoporosis. *J Bone Miner Res.* 2004;19(8):1241-1249.	Experimental-Dx	2,946 osteoporotic women	To prospectively show antifracture efficacy for the intermittent administration of a bisphosphonate.	After 3 years, the rate of new VFs was significantly reduced in patients receiving oral daily (4.7%) and intermittent ibandronate (4.9%), relative to placebo (9.6%). Thus, daily and intermittent oral ibandronate significantly reduced the risk of new morphometric VFs by 62% (P=0.0001) and 50% (P=0.0006), respectively, vs placebo. Both treatment groups also produced a statistically significant relative risk reduction in clinical VFs (49% and 48% for daily and intermittent ibandronate, respectively). Significant and progressive increases in lumbar spine (6.5%, 5.7%, and 1.3% for daily ibandronate, intermittent ibandronate, and placebo, respectively, at 3 years) and hip BMD, normalization of bone turnover, and significantly less height loss than in the placebo group were also observed for both ibandronate regimens. The overall population was at low risk for osteoporotic fractures. Consequently, the incidence of non-VFs was similar between the ibandronate and placebo groups after 3 years (9.1%, 8.9%, and 8.2% in the daily, intermittent, and placebo groups, respectively; difference between arms not significant). However, findings from a posthoc analysis showed that the daily regimen reduces the risk of non-VFs (69%; P=0.012) in a higher-risk subgroup (femoral neck BMD T score < -3.0). In addition, oral ibandronate was well tolerated. Oral ibandronate, whether administered daily or intermittently with an extended between-dose interval of >2 months, is highly effective in reducing the incidence of osteoporotic fractures in postmenopausal women.	1

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
51. Kanis JA, Barton IP, Johnell O. Risedronate decreases fracture risk in patients selected solely on the basis of prior vertebral fracture. *Osteoporos Int.* 2005;16(5):475-482.	Review/Other-Dx	1,802 patients	To examine the effects of risedronate (5 mg/daily) in patients identified solely on the basis of a prior fragility fracture, without BMD as an inclusion criterion.	Over 3 years, risedronate reduced the risk of new VFs by 44% (95% CI, 28% to 56%) compared with placebo. In patients subgrouped according to the presence or absence of putative risk factors, the efficacy of risedronate was comparable across all groups (all treatment-by-non BMD subgroup interactions $P \geq 0.210$). Adjustment for age, baseline BMD, and prevalent VFs on fracture risk gave results similar to the unadjusted analysis. In patients taking placebo, the incidence of new VF was higher in several of the high-risk categories (elderly, T-score ≤ -2.5 SD).	4
52. Neer RM, Arnaud CD, Zanchetta JR, et al. Effect of parathyroid hormone (1-34) on fractures and bone mineral density in postmenopausal women with osteoporosis. *N Engl J Med.* 2001;344(19):1434-1441.	Experimental-Tx	1,637 postmenopausal women	To determine the effect of parathyroid hormone (1-34) on fractures and BMD in postmenopausal women with osteoporosis.	New VFs occurred in 14% of the women in the placebo group and in 5% and 4%, respectively, of the women in the 20-microg and 40-microg parathyroid hormone groups; the respective relative risks of fracture in the 20-microg and 40-microg groups, as compared with the placebo group, were 0.35 and 0.31 (95% CIs, 0.22 to 0.55 and 0.19 to 0.50). New nonvertebral fragility fractures occurred in 6% of the women in the placebo group and in 3% of those in each parathyroid hormone group (relative risk, 0.47 and 0.46, respectively [95% CIs, 0.25 to 0.88 and 0.25 to 0.861). As compared with placebo, the 20-microg and 40-microg doses of parathyroid hormone increased BMD by 9 and 13 more percentage points in the lumbar spine and by 3 and 6 more percentage points in the femoral neck; the 40-microg dose decreased BMD at the shaft of the radius by 2 more percentage points. Both doses increased total-body bone mineral by 2 to 4 more percentage points than did placebo. Parathyroid hormone had only minor side effects (occasional nausea and headache).	1

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
53. Quandt SA, Thompson DE, Schneider DL, Nevitt MC, Black DM. Effect of alendronate on vertebral fracture risk in women with bone mineral density T scores of-1.6 to -2.5 at the femoral neck: the Fracture Intervention Trial. *Mayo Clin Proc.* 2005;80(3):343-349.	Experimental-Tx	3,737 postmenopausal women	To determine the efficacy of alendronate treatment on risk of VF in a subgroup of women from the Fracture Intervention Trial who had BMD T scores between -1.6 and -2.5 at the femoral neck and to describe how soon after initiation of therapy alendronate becomes effective and whether it is consistent in women with and without existing radiographic VF.	A total of 3,737 postmenopausal women were included in the study, 1,878 in the alendronate group and 1,859 in the placebo group. Risk of VF was significantly reduced by alendronate compared with placebo for clinical (relative risk, 0.40; 95% CI, 0.19–0.76; *P*=.005) and radiographic (RR, 0.57; 95% CI, 0.41–0.81; *P*=-.002) fracture. The reductions in VF risk were consistent in women with and without an existing radiographic VF for clinical (RR, 0.34; 95% CI, 0.12–0.84; and RR, 0.46; 95% CI, 0.16–1.17; respectively) and radiographic (RR, 0.53; 95% CI, 0.34–0.82; and RR, 0.64; 95% CI, 0.38–1.10; respectively) fractures. In both groups, the effect of alendronate on clinical VF was noted soon after therapy was initiated. The absolute risk of VF was low in women without a baseline radiographic fracture.	1
54. Cosman F, de Beur SJ, LeBoff MS, et al. Clinician's Guide to Prevention and Treatment of Osteoporosis. *Osteoporos Int.* 2014;25(10):2359-2381.	Review/Other-Dx	N/A	A clinician's guide to prevention and treatment of osteoporosis. This guide offers concise recommendations regarding prevention, risk assessment, diagnosis, and treatment of osteoporosis in postmenopausal women and men age 50 and older.	N/A	4
55. Lewiecki EM, Watts NB, McClung MR, et al. Official positions of the international society for clinical densitometry. *J Clin Endocrinol Metab.* 2004;89(8):3651-3655.	Review/Other-Dx	N/A	Official positions of the ISCD. The report summarizes the methodology of the ISCD PDC and presents selected Official Positions of general interest.	N/A	4
56. Adams JE. Quantitative computed tomography. *Eur J Radiol.* 2009;71(3):415-424.	Review/Other-Dx	N/A	A review on QCT.	No results stated.	4
57. Baran DT, Faulkner KG, Genant HK, Miller PD, Pacifici R. Diagnosis and management of osteoporosis: guidelines for the utilization of bone densitometry. *Calcif Tissue Int.* 1997;61(6):433-440.	Review/Other-Dx	N/A	Guidelines on the diagnosis and management of osteoporosis.	N/A	4

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
58. Hans D, Krieg MA, Lamy O, Felsenberg D. Beneficial Effects Of Strontium Ranelate Compared To Alendronate On Trabecular Bone Score In Post Menopausal Osteoporotic Women: A 2-Year Study. Paper presented at: Osteoporosis International 2012.	Observational-Tx	79 women	To compare the effects of strontium ranelate and alendronate on lumbar spine architecture patterns as assessed by TBS in women with postmenopausal osteoporosis.	Cross-calibration between sites using a TBS specific phantom did not show significant difference. Longtitudinal QC did not demonstrate any clinical relevant drift or shift over the study duration.	2
59. Kalder M, Hans D, Kyvernitakis I, Lamy O, Bauer M, Hadji P. Effects of Exemestane and Tamoxifen treatment on bone texture analysis assessed by TBS in comparison with bone mineral density assessed by DXA in women with breast cancer. *J Clin Densitom.* 2014;17(1):66-71.	Experimental-Tx	36 women randomized to receive tamoxifen (n = 17) or exemestane (n = 19)	An analysis of a substudy of the randomized Tamoxifen Exemestane Adjuvant Multinational trial to determine the effects of exemestane and tamoxifen adjuvant treatment on BMD measured by DXA compared with the TBS, a novel grey-level texture measurement that correlates with 3-D parameters of bone texture in postmenopausal women with hormone receptor-positive breast cancer for the first time.	Patients receiving tamoxifen showed a mean increase of BMD in lumbar spine from baseline of 1.0%, 1.5%, and 1.9% and in TBS of 2.2%, 3.5%, and 3.3% at 6-, 12-, and 24-months treatment, respectively. Conversely, patients receiving exemestane showed a mean decrease from baseline in LS-BMD of -2.3%, -3.6%, and -5.3% and in TBS of -0.9%, -1.7%, and -2.3% at 6-, 12-, and 24-months treatment, respectively. Changes in TBS from baseline at spine were also significantly different between exemestane and tamoxifen: P=0.05, 0.007, and 0.006 at 6, 12, and 24 months, respectively. Tamoxifen induced an increase in BMD and bone texture analysis, whereas exemestane resulted in decreases. The results were independent from each other.	1
60. Krieg MA, Aubry-Rozier B, Hans D, Leslie WD. Effects of anti-resorptive agents on trabecular bone score (TBS) in older women. *Osteoporos Int.* 2013;24(3):1073-1078.	Observational-Tx	534 treated women and 1,150 untreated	To evaluate the longitudinal effects of anti-resorptive agents (534 treated women vs 1,150 untreated) on LS- BMD and TBS.	1,150 untreated women and 534 treated women met the inclusion criteria. Only a weak correlation was seen between BMD and TBS in either group. Significant intergroup differences in BMD change and TBS change were observed over the course of follow-up (P<0.001). Similar mean decreases in BMD and TBS (-0.36%/year and -0.31%/year, respectively) were seen for untreated subjects (both P<0.001). Conversely, treated subjects exhibited a significant mean increase in BMD (+1.86%/year, P<0.002) and TBS (+0.20%/year, P<0.001). TBS is responsive to treatment with non-estrogen anti- resorptive drug therapy in women over age 50. The treatment-related increase in TBS is less than the increase in BMD, which is consistent with bone texture preservation.	2

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
61. Popp AW, Guler S, Lamy O, et al. Effects of zoledronate versus placebo on spine bone mineral density and microarchitecture assessed by the trabecular bone score in postmenopausal women with osteoporosis: a three-year study. *J Bone Miner Res.* 2013;28(3):449-454.	Observational-Tx	107 patients randomly assigned to either zoledronate (n = 54) or placebo (n = 53)	To compare the effects of yearly intravenous zoledronate vs placebo on LS-BMD and TBS in postmenopausal women with osteoporosis.	Baseline characteristics (mean +/- SD) were similar between groups in terms of age, 76.8 +/- 5.0 years; BMI, 24.5 +/- 3.6 kg/m(2) ; TBS, 1.178 +/- 0.1 but for LS T-score (zoledronate -2.9 +/- 1.5 vs placebo -2.1 +/- 1.5). Changes in LS-BMD were significantly greater with zoledronate than with placebo at all-time points (P<0.0001 for all), reaching +9.58% vs +1.38% at month 36. Change in TBS was significantly greater with zoledronate than with placebo as of month 24, reaching +1.41 vs -0.49% at month 36; P=0.031, respectively. LS-BMD and TBS were weakly correlated (r = 0.20) and there were no correlations between changes in BMD and TBS from baseline at any visit. In postmenopausal women with osteoporosis, once-yearly intravenous zoledronate therapy significantly increased LS-BMD relative to placebo over 3 years and TBS as of 2 years.	1
62. Cohen A, Lang TF, McMahon DJ, et al. Central QCT reveals lower volumetric BMD and stiffness in premenopausal women with idiopathic osteoporosis, regardless of fracture history. *J Clin Endocrinol Metab.* 2012;97(11):4244-4252.	Observational-Dx	32 premenopausal women with idiopathic osteoporosis, 12 with idiopathic low BMD, and 34 controls	To compare 3D volumetric BMD and bone stiffness in premenopausal women with idiopathic osteoporosis based on fracture history, those with idiopathic low BMD (Z score ≤ -2.0) and no low trauma fracture, and normal age-matched controls.	Subjects had comparable decreases in total and trabecular volumetric BMD, cortical thickness, and whole-bone stiffness compared with controls, regardless of fracture history. These differences remained significant after controlling for age, BMI, and bone size. The positive predictive values of a DXA Z score of -2.0 or less for a central QCT volumetric BMD Z score of -2.0 or less were 95% at the lumbar spine, 90% at the total hip, and 86% at the femoral neck.	3

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
63. Liu XS, Cohen A, Shane E, et al. Bone density, geometry, microstructure, and stiffness: Relationships between peripheral and central skeletal sites assessed by DXA, HR-pQCT, and cQCT in premenopausal women. *J Bone Miner Res.* 2010;25(10):2229-2238.	Review/Other-Dx	69 premenopausal women	The authors performed a DXA, central QCT, HR-pQCT, and image-based finite-element analyses on 69 premenopausal women to evaluate relationships among cortical and trabecular bone density, geometry, microstructure, and stiffness of the lumbar spine, proximal femur, distal radius, and distal tibia.	Significant correlations were found between the stiffness of the 2 peripheral sites (r = 0.86), 2 central sites (r = 0.49), and between the peripheral and central skeletal sites (r = 0.56-0.70). These associations were explained in part by significant correlations in areal bone mineral density, volumetric bone mineral density, and cross-sectional area between the multiple skeletal sites. For the prediction of proximal femoral stiffness, volumetric BMD (r = 0.75) and stiffness (r = 0.69) of the distal tibia by HR-pQCT were comparable with direct measurements of the proximal femur: areal BMD of the hip by DXA (r = 0.70) and volumetric BMD of the hip by central QCT (r = 0.64). For the prediction of vertebral stiffness, trabecular volumetric BMD (r = 0.58) and stiffness (r = 0.70) of distal radius by HR-pQCT were comparable with direct measurements of lumbar spine: areal BMD by DXA (r = 0.78) and volumetric BMD by central QCT (r = 0.67).	4
64. Cohen A, Dempster DW, Muller R, et al. Assessment of trabecular and cortical architecture and mechanical competence of bone by high-resolution peripheral computed tomography: comparison with transiliac bone biopsy. *Osteoporos Int.* 2010;21(2):263-273.	Observational-Dx	54 subjects	To determine the extent to which microarchitectural variables measured by HR-pQCT reflect those measured by the "gold standard," transiliac bone biopsy.	The strongest correlations observed were between trabecular parameters (bone volume fraction, number, separation) measured by microCT of biopsies and HR-pQCT of the radius (R 0.365-0.522; $P<0.01$). Cortical width of biopsies correlated with cortical thickness by HR-pQCT, but only at the tibia (R = 0.360, $P<0.01$). Apparent Young's modulus calculated by microFE of biopsies correlated with that calculated for both radius (R = 0.442; $P<0.001$) and tibia (R = 0.380; $P<0.001$) HR-pQCT scans.	3

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
65. Adami S, Giannini S, Giorgino R, et al. Effect of age, weight and lifestyle factors on calcaneal quantitative ultrasound in premenopausal women: the ESOPO study. *Calcif Tissue Int.* 2004;74(4):317-321.	Review/Other-Dx	2,727 premenopausal women	To identify the determinants of bone mass as measured by QUS in premenopausal women.	The most commonly recognized determinants of bone mass were modelled with stiffness by multiple regression analysis or analysis of variance. Bone stiffness was negatively related to age and number of cigarettes and positively to body weight, body weight at 25 years, height and estimated daily calcium intake. By multiple regression analysis, independent, positive, predictors of bone stiffness were age, weight at 25 years and daily calcium intake. Bone stiffness adjusted for age and body weight at 25 years was positively associated with outdoor activity score and negatively with number of pregnancies, chronic use of any drug, smoking and subjective health status. Bone stiffness was also somewhat ($P<0.015$) negatively related to history of prolonged bedrest and thyroxin use.	4
66. Link TM, Lang TF. Axial QCT: clinical applications and new developments. *J Clin Densitom.* 2014;17(4):438-448.	Review/Other-Dx	N/A	A review on the clinical applications and new developments of axial QCT.	Compared with DXA, the current standard BMD technique, QCT has a number of pertinent advantages, including volumetric measurements, less susceptibility to degenerative spine changes, and higher sensitivity to changes in bone mass. Disadvantages include the higher radiation doses and less experience with fracture prediction and therapy monitoring. Over the last 10 years, a number of novel applications have been described allowing assessment of BMD and bone quality in larger patient populations, developments that may substantially improve patient care.	4
67. Delmas PD, van de Langerijt L, Watts NB, et al. Underdiagnosis of vertebral fractures is a worldwide problem: the IMPACT study. *J Bone Miner Res.* 2005;20(4):557-563.	Observational-Dx	2,451 postmenopausal women	To assess prospectively and globally the accuracy of the spinal radiographic diagnosis of VFs by comparing results of local radiographic reports with that of subsequent central readings.	Of 2,451 women with an evaluable radiograph both centrally and locally, 789 (32%) had at least one VF. Adjudicated discrepancies (n = 350 patients) between local and central readings because of undetected VF (68%) or equivocal terminology in the local radiology report (32%) yielded a false-negative rate of 34%.	3

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
68. Fechtenbaum J, Cropet C, Kolta S, Verdoncq B, Orcel P, Roux C. Reporting of vertebral fractures on spine X-rays. *Osteoporos Int.* 2005;16(12):1823-1826.	Observational-Dx	824 patients	To compare the identification of VFs on spine X-rays among rheumatologists.	In 629 patients (among 824 included) at least one VF was diagnosed, and the X-rays were then sent to a central facility where a semi-quantitative assessment of VF was performed by a single rheumatologist trained for this evaluation. According to the vertebral level, kappa scores were between 0.20 to 0.77, i.e., below 0.6 from T4 to T7, and between 0.6 and 0.77 from T8 to L4. The false-negative fractures rate was 25.8% (and 15.7% of them were related to a numbering discrepancy). The rate of false positive fractures was 6.3%. At the patient level 6.8% had actually no fracture. This study shows that 25% of overall VFs are not diagnosed among patients considered as having at least one fracture. As a consequence, patients who require treatment to reduce fracture risk are not being properly identified.	3
69. Lenchik L, Rogers LF, Delmas PD, Genant HK. Diagnosis of osteoporotic vertebral fractures: importance of recognition and description by radiologists. *AJR Am J Roentgenol.* 2004;183(4):949-958.	Review/Other-Dx	N/A	To review the diagnosis of osteoporotic VFs.	No results stated.	4
70. Nunez DB, Jr., Zuluaga A, Fuentes-Bernardo DA, Rivas LA, Becerra JL. Cervical spine trauma: how much more do we learn by routinely using helical CT? *Radiographics.* 1996;16(6):1307-1318; discussion 1318-1321.	Review/Other-Dx	88 patients	To evaluate the nature, location, and clinical significance of the fractures that were missed at plain radiography.	Of the 88 patients, 32 patients had cervical spine fractures (n = 50) that were not revealed or were incompletely demonstrated at radiography. Most missed fractures occurred at the C-1 to C-2 and C-6 to C-7 levels, and most involved the transverse processes and the posterolateral elements of the vertebrae. One-third of the patients with missed fractures had either clinically significant or unstable injuries, as determined on the basis of mechanistic or imaging criteria. Helical CT can depict significant fractures not shown by plain radiography and should be added routinely to the initial screening for cervical spine fractures in polytrauma victims.	4

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
71. Chan JH, Peh WC, Tsui EY, et al. Acute vertebral body compression fractures: discrimination between benign and malignant causes using apparent diffusion coefficients. *Br J Radiol.* 2002;75(891):207-214.	Observational-Dx	32 patients	To perform MRI on patients with acute vertebral body compression fractures with the single shot echo planar diffusion weighted pulse sequence and to evaluate the usefulness of apparent diffusion coefficient values in differentiating between vertebral body compression fractures caused by either tumor infiltration (malignant) or solely trauma (benign).	Signal intensities on T(1) weighted, short tau inversion recovery and diffusion weighted images were compared. Apparent diffusion coefficient values of normal and abnormal vertebral bodies were calculated. Except for two patients with sclerotic metastases, benign acute VFs were hypointense and malignant acute VFs were hyperintense with respect to normal bone marrow on diffusion weighted images. Mean combined apparent diffusion coefficients; average of the combined apparent diffusion coefficients in the x, y and z diffusion directions) were 0.23 x 10(-3) mm(2) s(-1) in normal vertebrae, 0.82 x 10(-3) mm(2) s(-1) in malignant acute VFs and 1.94 x 10(-3) mm(2) s(-1) in benign acute VFs. The differences between mean combined apparent diffusion coefficients values were statistically significant ($P<0.001$).	3
72. Fu TS, Chen LH, Liao JC, Lai PL, Niu CC, Chen WJ. Magnetic resonance imaging characteristics of benign and malignant vertebral fractures. *Chang Gung Med J.* 2004;27(11):808-815.	Observational-Dx	48 patients with malignant VFs and 50 patients with benign processes	To analyze and determine which conventional MRI parameters are useful for the early differentiation between benign and malignant VFs.	Lesions with negative gadolinium enhancement were favored as benign fractures. A uniform signal change in multiple involved vertebra lesions, round, smooth margins with marked epidural compression, a paraspinal soft tissue mass, and pedicle and posterior element involvement were probable malignant characteristics. Among them an associated paraspinal soft tissue mass was found to be significant in predicting the probability of malignancy.	3
73. Uetani M, Hashmi R, Hayashi K. Malignant and benign compression fractures: differentiation and diagnostic pitfalls on MRI. *Clin Radiol.* 2004;59(2):124-131.	Review/Other-Dx	N/A	To illustrate the MRI features of malignant and benign compression fractures with emphasis on the usefulness, limitations and pitfalls of MRI.	No results stated.	4

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
74. Abdel-Wanis ME, Solyman MT, Hasan NM. Sensitivity, specificity and accuracy of magnetic resonance imaging for differentiating vertebral compression fractures caused by malignancy, osteoporosis, and infections. *J Orthop Surg (Hong Kong).* 2011;19(2):145-150.	Observational-Dx	80 patients	To evaluate the sensitivity, specificity and accuracy of various MRI features in differentiating vertebral compression fractures caused by malignancy, osteoporosis, and infections.	The MRI diagnosis was correct in 78 and inconclusive in 2 with malignancy. MRI features suggestive of malignant fractures were a convex posterior border of the vertebral body, pedicle involvement, posterior neural element involvement, an epidural mass, a paraspinal mass, and other spinal metastases. MRI features suggestive of osteoporotic fractures were retropulsion, low signal intensity band, spared normal marrow signal intensity, and the fluid sign. MRI features suggestive of infective fractures were contiguous vertebral involvement, end plate disruption, disc involvement, and paraspinal and epidural abscesses.	3
75. Choi WH, Oh SH, Lee CJ, Rhim JK, Chung BS, Hong HJ. Usefulness of SPAIR Image, Fracture Line and the Adjacent Discs Change on Magnetic Resonance Image in the Acute Osteoporotic Compression Fracture. *Korean J Spine.* 2012;9(3):227-231.	Observational-Dx	85 patients	To evaluate the usefulness of SPAIR image, fracture line and the adjacent discs change on MRI in the acute osteoporotic compression fracture.	In this study, the incidence of high signal intensity on T2-SPAIR image was very high (0.9917). The fluid sign was seen in 56.7% on the SPAIR image. The fracture lines were more observed on the T2WI than T1WI (P=0.0062). The adjacent discs change on T2WI and T2-SPAIR image were higher than T1WI (P<0.001).	3

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
76. Ferrar L, Jiang G, Eastell R, Peel NF. Visual identification of vertebral fractures in osteoporosis using morphometric X-ray absorptiometry. *J Bone Miner Res.* 2003;18(5):933-938.	Observational-Dx	70 women	To (1) compare quantitative and visual assessment of MXA scans with visual assessment of spinal radiographs for the identification of prevalent and incident VFs; (2) compare visual assessment of MXA scans and spinal radiographs made by the same observer for the identification of prevalent and incident VFs; and (3) test interobserver agreement between expert readers for visual assessment of MXA scans and spinal radiographs.	Sensitivity for the identification of prevalent fractures by MXA was best for visual MXA by observer A (92%), whereas quantitative MXA had the lowest sensitivity (82%). Specificity was >90% for both visual and quantitative MXA. Kappa scores for agreement for identification of prevalent fractures between visual XR (observer A) and visual MXA (all 3 observers), and between visual X-ray and visual MXA performed by reader B were similar (kappa = 0.85-0.87). Agreement with visual X-ray performed by observer A was slightly lower for quantitative MXA (kappa = 0.77). Interobserver agreement between the 2 expert readers (observers A and B) was the same for both visual X-ray and visual MXA (kappa = 0.86). 7 incident VFs were identified in 4 patients at follow-up. All 4 patients were identified by visual MXA, and 3 patients were identified by quantitative MXA. Observers A and B identified all 7 incident fractures by visual MXA, and observer C missed 1 fracture that was also missed by quantitative MXA. An incident fracture of vertebra T6 was excluded from analysis by quantitative MXA because of poor image quality.	3

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
77. Rea JA, Chen MB, Li J, et al. Morphometric X-ray absorptiometry and morphometric radiography of the spine: a comparison of prevalent vertebral deformity identification. *J Bone Miner Res*. 2000;15(3):564-574.	Observational-Dx	161 postmenopausal women	To report a direct comparison of prevalent vertebral deformity identification using quantitative morphometric techniques on the MXA scans and conventional radiographic images acquired on a group of postmenopausal women, ranging from healthy individuals with "normal" bone density to subjects with severe osteoporosis and multiple vertebral deformities.	Deformity identification by MXA was limited because of poor image quality, primarily in the upper thoracic spine. One in 6 MRX deformities were missed by MXA as they occurred in vertebrae not visualized sufficiently for analysis on the MXA scans. Deformity identification was poorer in the upper thoracic spine in analyzable vertebrae with a sensitivity of 50.0% for MXA in terms of MRX using the Eastell algorithm for the vertebral levels T4–T7, compared with 80.6% for L1–L4. MXA proved to be more effective at identifying moderate to severe MRX deformities producing a sensitivity of 22.0% for MXA in terms of identifying MRX grade 1 deformities using the Eastell algorithm, compared with 81.6% for grade 2 deformities.	3
78. Binkley N, Krueger D, Gangnon R, Genant HK, Drezner MK. Lateral vertebral assessment: a valuable technique to detect clinically significant vertebral fractures. *Osteoporos Int.* 2005;16(12):1513-1518.	Observational-Dx	80 postmenopausal women	To evaluate the ability of clinicians using lateral vertebral assessment to detect prevalent VFs.	Using lateral vertebral assessment, 95% of vertebral bodies from T7 through L4 were evaluable, but a majority (66%) of vertebrae from T4 to T6 were not adequately visualized. In the lateral vertebral assessment-evaluable vertebrae, prevalent fractures were identified in 40 vertebral bodies by radiography. In this regard, the clinicians using lateral vertebral assessment detected 17/18 radiographically evident VFs of grade 2 or 3, a false negative rate of 6%. They identified 50% (11/22) of grade 1 fractures. Additionally, the vast majority of evaluable nonfractured vertebrae, (764/794, 96.2%) were correctly classified as normal by lateral vertebral assessment. Thus, clinicians utilizing lateral vertebral assessment correctly identified the vast majority of grade 2 or 3 vertebral compression fractures and normal vertebral bodies, although detection of grade 1 fractures was less effective.	3

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
79. Ferrar L, Jiang G, Clowes JA, Peel NF, Eastell R. Comparison of densitometric and radiographic vertebral fracture assessment using the algorithm-based qualitative (ABQ) method in postmenopausal women at low and high risk of fracture. *J Bone Miner Res.* 2008;23(1):103-111.	Observational-Dx	755 postmenopausal women	To (1) calculate agreement between VFA and radiography using the algorithm-based qualitative method to identify prevalent VFs and (2) determine the primary reasons for any discrepancies in diagnosis between VFA and radiography.	The prevalence of VF was 11%–29% (radiography) and 9%–26% (VFA) in the low-risk and high-risk groups, respectively. Agreement between imaging modalities was good or very good (kappa = 0.62-0.81 in the low-risk and high-risk populations). The sensitivity to detect women with VF by VFA was 71% and 84% in the low-risk and high-risk populations, respectively, and specificity was 97%. 52 (77%) and 60 (61%) of vertebrae misclassified by VFA in the low-risk and high-risk populations were mild fractures and 37 (54%) and 62 (63%) were wedge fractures. One third of fractures missed by VFA were related to poor or unreadable image quality (n = 27 and 28 vertebrae in the low-risk and high-risk populations, respectively).	2

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
80. Shane E, Burr D, Ebeling PR, et al. Atypical subtrochanteric and diaphyseal femoral fractures: report of a task force of the American Society for Bone and Mineral Research. *J Bone Miner Res.* 2010;25(11):2267-2294.	Review/Other-Dx	N/A	To summarize the findings and recommendations of the task force on the American Society for Bone and Mineral Research.	Based on published and unpublished data and the widespread use of bisphosphonates, the incidence of atypical femoral fractures associated with BP therapy for osteoporosis appears to be very low, particularly compared with the number of vertebral, hip, and other fractures that are prevented by bisphosphonates. Moreover, a causal association between bisphosphonates and atypical fractures has not been established. However, recent observations suggest that the risk rises with increasing duration of exposure, and there is concern that lack of awareness and underreporting may mask the true incidence of the problem. Given the relative rarity of atypical femoral fractures, the task force recommends that specific diagnostic and procedural codes be created and that an international registry be established to facilitate studies of the clinical and genetic risk factors and optimal surgical and medical management of these fractures. Physicians and patients should be made aware of the possibility of atypical femoral fractures and of the potential for bilaterality through a change in labeling of bisphosphonates. Research directions should include development of animal models, increased surveillance, and additional epidemiologic and clinical data to establish the true incidence of and risk factors for this condition and to inform orthopedic and medical management.	4
81. Compston J. Pathophysiology of atypical femoral fractures and osteonecrosis of the jaw. *Osteoporos Int.* 2011;22(12):2951-2961.	Review/Other-Dx	N/A	To review pathophysiology of atypical femoral fractures and osteonecrosis of the jaw.	No results stated in abstract.	4
82. van der Meulen MC, Boskey AL. Atypical subtrochanteric femoral shaft fractures: role for mechanics and bone quality. *Arthritis Res Ther.* 2012;14(4):220.	Review/Other-Dx	N/A	To discuss the use of bisphosphonates, their effects on bone remodeling, mechanics and tissue composition, their significance as an effective therapy for osteoporosis, and why these agents may increase fracture risk in a small population of patients.	No results stated.	4

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
83. Rosenberg ZS, La Rocca Vieira R, Chan SS, et al. Bisphosphonate-related complete atypical subtrochanteric femoral fractures: diagnostic utility of radiography. *AJR Am J Roentgenol.* 2011;197(4):954-960.	Observational-Dx	One group treated with bisphosphonates (19 fractures in 17 patients) and second group not treated with bisphosphonates (19 fractures in in 19 patients)	To evaluate the diagnostic utility of conventional radiography for diagnosing bisphosphonate-related atypical subtrochanteric femoral fractures.	Among the candidate predictors of bisphosphonate-related fractures, focal lateral cortical thickening and transverse fracture had the highest ORs (76.4 and 10.1, respectively). Medial spike and comminution had ORs of 3.8 and 0.63, respectively. Focal lateral cortical thickening and transverse fracture were also the most accurate factors for detecting bisphosphonate-related fractures for all readers. The sensitivity, specificity, and overall accuracy for diagnosing bisphosphonate-related fractures were 94.7%, 100%, and 97.4% for reader 1; 94.7%, 68.4%, and 81.6% for reader 2; and 89.5%, 89.5%, and 89.5% for reader 3, respectively. The interobserver agreement was substantial (kappa >0.61).	2
84. Capeci CM, Tejwani NC. Bilateral low-energy simultaneous or sequential femoral fractures in patients on long-term alendronate therapy. *J Bone Joint Surg Am.* 2009;91(11):2556-2561.	Review/Other-Dx	7 patients	The authors retrospectively reviewed the case log of the senior author over the last 4 years to identify patients who presented with a subtrochanteric or diaphyseal femoral fracture after a low-energy mechanism of injury (a fall from standing height or less) and who had been taking alendronate for more than 5 years.	7 patients who sustained low-energy bilateral subtrochanteric or diaphyseal femoral fractures while on long-term alendronate therapy were identified. One patient presented with simultaneous bilateral diaphyseal fractures, 2 patients had sequential subtrochanteric fractures, and 4 patients had impending contralateral subtrochanteric stress fractures noted at the time of the initial fracture. Of the latter 4, 1 patient had a fracture through the stress site and the other 3 patients had prophylactic stabilization of the site with internal fixation. No patient had discontinued alendronate therapy prior to the second fracture. All patients were women with an average age of 61 years, and they had been on alendronate therapy for an average of 8.6 years. All fractures were treated with reamed intramedullary nailing and went on to union at an average of 4 months.	4

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
85. Kim S, Yang KH, Lim H, et al. Detection of prefracture hip lesions in atypical subtrochanteric fracture with dual-energy x-ray absorptiometry images. *Radiology.* 2014;270(2):487-495.	Observational-Dx	52 hips in 46 patients	To retrospectively assess how often and how early hip DXA images show prefracture lesions in patients with atypical subtrochanteric fracture and determine whether DXA images with assessment of prodromal symptoms could be used for early atypical subtrochanteric fracture prediction.	Overall detection rates for DXA, prodromal symptoms, and DXA with prodromal symptoms were 61% (20/33), 42% (14/33), and 73% (24/33), respectively, in the ipsilateral group. Overall detection rate comparisons showed that DXA with prodromal symptoms was superior to prodromal symptoms alone (P=.0377). The cumulative detection rate curve for DXA with prodromal symptoms was also superior to that of prodromal symptoms alone (P=.0018). Sensitivity and specificity of DXA in atypical subtrochanteric fracture prediction ranged from 52% (17/33) to 58% (19/33) and 99% (197/199) to 100% (199/199), respectively.	2
86. McKenna MJ, van der Kamp S, Heffernan E, Hurson C. Incomplete atypical femoral fractures: assessing the diagnostic utility of DXA by extending femur length. *J Clin Densitom.* 2013;16(4):579-583.	Review/Other-Dx	257 patients	To determine whether extending the length of the femur image at the time of DXA may diagnose an incomplete atypical femoral fractures.	Abnormal DXA images were suggested in 19/257 patients (7.4%). On X-ray, 7 patients (2.7%) showed no abnormality, 7 patients (2.7%) showed evidence of atypical femoral fracture, and 5 patients (2.0%) showed an unrelated radiographic abnormality. Of the 7 cases with X-ray evidence of atypical femoral fracture, 5 had a periosteal flare and 2 had a visible fracture line, both of whom needed insertion of an intramedullary nail.	4
87. Cheung AM, Bleakney R, Ridout R, et al. Detection of Incomplete Non-Displaced Atypical Femur Fractures by Densitometer. *Journal of Clinical Densitometry.* 2014;17(3):418.	Observational-Dx	144 subjects with 195 femurs	A cross-sectional study was performed to test the operating characteristics of single energy femur scans by densitometer to detect incomplete atypical femoral fractures.	The operating characteristics of single energy femur scans are presented in Table 1. For single energy femur scans, kappa was highest for presence of lucent cleft [0.63, 95% CI (0.37–0.90)], followed by focal cortical thickening [0.55, (0.38–0.72)]. For conventional radiographs, kappa was highest for focal cortical thickening [0.61, (0.43–0.78)], followed by endosteal thickening [0.53, (0.30–0.76)].	2

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
88. Ahlman MA, Rissing MS, Gordon L. Evolution of bisphosphonate-related atypical fracture retrospectively observed with DXA scanning. *J Bone Miner Res.* 2012;27(2):496-498.	Review/Other-Dx	1 patient	The authors present a case of a 61-year-old female with history of long-term bisphosphonate therapy for osteoporosis initially diagnosed by screening DXA.	This case is presented to show that a common location and classic appearance of subtrochanteric bisphosphonate-associated fractures may be clearly visualized on absorptiometry images long before fracture. This observation is important because the majority of patients taking bisphosphonate therapy also receive regular DXA imaging. Because of the chronicity of standard bone-density monitoring for these patients throughout their treatment regimen, DXA may find a role for early detection of cortical abnormalities.	4
89. Chan SS, Rosenberg ZS, Chan K, Capeci C. Subtrochanteric femoral fractures in patients receiving long-term alendronate therapy: imaging features. *AJR Am J Roentgenol.* 2010;194(6):1581-1586.	Review/Other-Dx	34 proximal femoral fractures in 22 patients	A paradoxical association between long-term alendronate therapy and low energy subtrochanteric femoral fractures has been recently recognized. A retrospective review of 34 such femoral fractures was performed.	Subtrochanteric femoral fractures associated with long-term alendronate therapy present with minimal trauma, may be chronic, and when incomplete may be missed. The characteristic imaging features include initial involvement and focal thickening of the lateral cortex, transverse orientation, medial beak, and superior displacement and varus angulation at the fracture site.	4

Evidence Table Key

Study Quality Category Definitions

- *Category 1* The study is well-designed and accounts for common biases.
- *Category 2* The study is moderately well-designed and accounts for most common biases.
- *Category 3* There are important study design limitations.
- *Category 4* The study is not useful as primary evidence. The article may not be a clinical study or the study design is invalid, or conclusions are based on expert consensus. For example:
  a) the study does not meet the criteria for or is not a hypothesis-based clinical study (e.g., a book chapter or case report or case series description);
  b) the study may synthesize and draw conclusions about several studies such as a literature review article or book chapter but is not primary evidence;
  c) the study is an expert opinion or consensus document.
- M = Meta-analysis

Dx = Diagnostic

Tx = Treatment

Abbreviations Key

AUC = Area under the receiver operating characteristic curve

BMD = Bone mineral density

BMI = Body mass index

CI = Confidence interval

CT = Computed tomography

DXA = Dual-energy X-ray absorptiometry

HR = Hazard ratio

HR-pQCT = High-resolution peripheral quantitative computed tomography

LS-BMD = Lumbar spine bone mineral density

MRI = Magnetic resonance imaging

MXA = Morphometric X-ray absorptiometry

OR = Odds ratio

PHPT = Primary hyperparathyroidism

pQCT = Peripheral quantitative computed tomography

QCT = Quantitative computed tomography

QUS = Quantitative ultrasound

RR= Risk ratio

SD = Standard deviation

TBS = Trabecular bone score

VFA = Vertebral fracture assessment

VF = Vertebral fracture