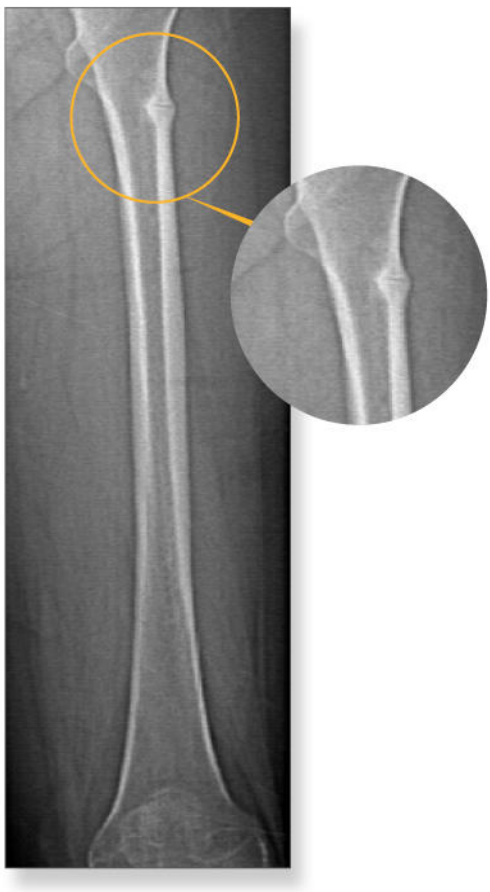
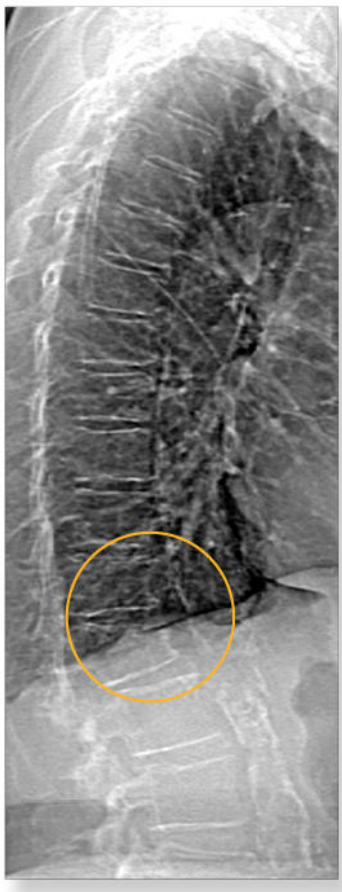
HOLOGIC®
The Science of Sure

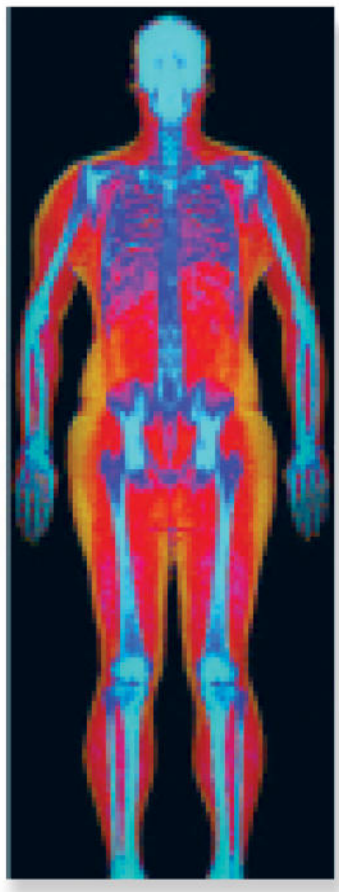
# Powerful images.
# **Clear answers.**



Manage Patient's concerns about Atypical Femur Fracture*



Vertebral Fracture Assessment – a critical part of a complete fracture risk assessment



Advanced Body Composition® Assessment – the power to see what's inside

**Contact your Hologic rep today at BSHSalesSupportUS@hologic.com**



*Incomplete Atypical Femur Fractures imaged with a Hologic densitometer, courtesy of Prof. Cheung, University of Toronto



**www.hologic.com | dxaperformance.com | 1.800.442.9892**

PERSPECTIVE

JBMR®

# Treated Osteoporosis Is Still Osteoporosis

E Michael Lewiecki,[1] Neil Binkley,[2] and John P Bilezikian[3]

[1]New Mexico Clinical Research & Osteoporosis Center, Albuquerque, NM, USA
[2]University of Wisconsin, Madison, WI, USA
[3]Columbia University College of Physicians and Surgeons, New York, NY, USA

Osteoporosis can be diagnosed by dual-energy X-ray absorptiometry (DXA) when bone mineral density (BMD) is at least 2.5 standard deviations below the mean BMD of a young-adult reference range (T-score $\leq -2.5$) at appropriate skeletal sites,[1,2] provided no other skeletal disease is responsible. Pharmacologic treatment to reduce fracture risk is commonly recommended for these patients and others at high risk for fracture, eg, those with prior osteoporotic fracture or those with high fracture risk according to risk calculators such as the Fracture Risk Assessment Tool (FRAX), the Garvan Fracture Risk Calculator, the simplified semiquantitative approach developed by the Canadian Association of Radiologists and Osteoporosis Canada (CAROC), and QResearch Database's QFractureScores.[3] Effective pharmacologic therapy can increase BMD and reduce fracture risk. When a subsequent DXA test shows improvement in T-score values to better than –2.5, the question arises, "Does the patient still have osteoporosis?" The answer is yes. We will explain why.

Failure to maintain the diagnosis of osteoporosis in individuals with a satisfactory DXA-measured BMD response to therapy can be detrimental to patient care. The following is an example of potential harm caused by a DXA report reclassifying a patient as osteopenic when she is being treated for osteoporosis.

> A 73-year-old Caucasian woman was diagnosed with osteoporosis because of a T-score of –2.8 at the left femoral neck. Lumbar spine could not be accurately measured because of osteoarthritic changes. She had lost 1.75 inches from her peak height. Spine imaging revealed a previously unrecognized T11 compression fracture with 30% vertebral height loss. Treatment was recommended. Alendronate was considered but not prescribed because of chronic kidney disease, stage 3b (estimated glomerular filtration rate 31 mL/min). She was started, instead, on denosumab 60 mg subcutaneously every 6 months. Two years later, a repeat DXA study showed a BMD improvement such that the left femoral neck T-score was –2.4. BMD T-scores at the total hip and 1/3 radius were also better than –2.5. The computer-assisted DXA interpretation, signed by a physician, was 'osteopenia, fracture risk is moderate.' The patient was pleased to read that she now had osteopenia, not osteoporosis. Her physician cautioned that treatment should be continued because fracture risk remained high; however, the health plan pharmacy benefits manager denied coverage of denosumab, stating that denosumab is not approved for treatment of patients with osteopenia.

The consequences of stopping treatment because of the insurance denial are potentially devastating. Discontinuation of denosumab is associated with a rapid BMD decline, return of vertebral fracture risk to baseline, and, even worse, an increase in the risk of multiple vertebral fractures, especially in patients with a prior vertebral fracture.[4] What went wrong?

1) Proper interpretation of DXA cannot be done exclusively by algorithm, especially when not fully informed with necessary data. Had the algorithm recognized the previous T-score of –2.8 and/or the documented vertebral fracture, it might have generated a report that retained the diagnosis of osteoporosis.
2) The DXA interpreter must consider all relevant clinical information obtained from the patient, the referring physician, and previous DXA studies, if available, before submitting a report. If the interpreter of this DXA had been aware that the previous DXA showed an osteoporotic T-score or that the patient had a documented vertebral fracture, perhaps the report would have still retained a diagnosis of osteoporosis.
3) The burden of retaining the diagnosis is ultimately with the treating physician, who in this case knew about the prior DXA diagnosis of osteoporosis and previous vertebral fracture. Retaining the diagnosis of osteoporosis is somewhat analogous to standard practice with patients having other chronic diseases: when treated or adequately controlled, the diagnosis persists. The diagnosis of hypertension or hyperlipidemia is not changed when effective treatment improves or normalizes the blood pressure or lipid status. Improvement in these quantitative parameters represents a favorable response to therapy, not elimination of the disease. Similarly, in diabetes mellitus, control of the blood glucose, even with normal hemoglobin A1c, does not change the diagnosis of diabetes mellitus. As with hypertension, hyperlipidemia, and diabetes, there is no current "cure" for osteoporosis.
4) It is unfortunately common that patients with osteoporosis are subsequently diagnosed with osteopenia according to

Received in original form December 11, 2018; revised form January 8, 2019; accepted January 11, 2019. Accepted manuscript online Month 00, 2018.
Address correspondence to: E Michael Lewiecki, MD, 300 Oak Street NE, Albuquerque, NM 87106, USA. E-mail mlewiecki@gmail.com
Journal of Bone and Mineral Research, Vol. 34, No. 4, Month 2019, pp 605–606.
DOI: 10.1002/jbmr.3671

T-score values being better than −2.5 in the most current DXA. This may occur because important clinical information is not known or the previous DXA is not available. We recommend that authoritative bodies, such as the International Society for Clinical Densitometry, clarify diagnostic criteria with follow-up DXA studies in treated patients. Until then, as noted above, it is the clinician who bears the responsibility to retain the diagnosis of osteoporosis and use the proper diagnostic codes.

Discontinuation of all therapies for osteoporosis, with the exception of the bisphosphonates, is followed by rapid loss of BMD and increased fracture risk without subsequent therapy. Stopping bisphosphonate therapy is also followed by loss of effect but at a slower pace than non-bisphosphonates. It is widely recognized that fracture risk is determined by many factors, including falls risk, low BMD, and non-BMD skeletal properties, such microarchitectural deterioration, a key element in the definition of osteoporosis.[5] Antiresorptive therapies do not restore degraded bone microarchitecture. Osteoanabolic therapies (eg, teriparatide, abaloparatide) may restore microstructure, at least partially, but the effect is rapidly lost after discontinuation if no other treatment is then given. This important concept emphasizes again that improving the T-score to better than −2.5 does not "cure" the disease or permanently change its fundamental properties. Thus, a decision to reclassify a patient because the T-score has improved to better than −2.5 is not warranted. Similarly, denial of coverage for therapy on this basis is also an unwise approach to patient care.

We emphasize the necessity of retaining the diagnosis of osteoporosis regardless of treatment response and change in BMD. This is not a trivial matter. Diagnostic classification may have important clinical implications in the perception of the disease, treatment decisions, and insurance coverage. For treated patients, a statistically significant increase in BMD, measured at a good-quality DXA facility, may represent an excellent response to treatment, reduction of fracture risk, and possibly achievement of a T-score target[6] but not a cure of the disease. Although the patient described here was treated with denosumab, the fundamental principles are the same with other medications, including bisphosphonates, osteoanabolic agents, raloxifene, and estrogen.

Current osteoporosis medications treat but do not cure the disease. Discontinuation of any of them is followed by loss of BMD at variable rates (ie, slow offset of effect with bisphosphonates, rapid offset with non-bisphosphonates), further degradation of bone microarchitecture, and increasing fracture risk. We believe that patient care is optimized when it is recognized by all stakeholders that osteoporosis does not disappear after it is treated, even when T-scores improve to better than −2.5. Successfully treated osteoporosis is still osteoporosis.

## Disclosures

EML reports research grant support from Amgen and Radius; consulting fees from Amgen, Radius, Shire, Alexion, Ultragenyx, and Sandoz; speaking fees from Radius, Shire, and Alexion; and board membership with the National Osteoporosis Foundation, the International Society for Clinical Densitometry, and the Osteoporosis Foundation of New Mexico. NB reports research grant support from Radius and consulting fees from Amgen and Taurus. JPB reports consulting fees from Amgen, Alexion, Abiogen, Shire, Radius, Ultragenyx, and Regeneron.

## Acknowledgments

No financial support was provided for the preparation, writing, and editing of this manuscript.

Authors' roles: All authors actively participated in the conception, development, planning, execution, and writing of the manuscript and all agree and accept responsibility for the contents of the manuscript.

## References

1. Kanis JA. Assessment of fracture risk and its application to screening for postmenopausal osteoporosis: synopsis of a WHO report. WHO Study Group. Osteoporos Int. 1994;4(6):368–81.
2. 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):274–86.
3. Leslie WD, Lix LM. Comparison between various fracture risk assessment tools. Osteoporos Int. 2014;25(1):1–21.
4. Cummings SR, Ferrari S, Eastell R, et al. Vertebral fractures after discontinuation of denosumab: a post hoc analysis of the randomized placebo-controlled FREEDOM trial and its extension. J Bone Miner Res. 2018;33(2):190–8.
5. Klibanski A, Adams-Campbell L, Bassford T, et al. Osteoporosis prevention, diagnosis, and therapy. JAMA. 2001;285(6):785–95.
6. Cummings SR, Cosman F, Lewiecki EM, et al. Goal-directed treatment for osteoporosis: a progress report from the ASBMR-NOF Working Group on Goal-Directed Treatment for Osteoporosis. J Bone Miner Res. 2017;32(1):3–10.