**Bringing osteoporosis up to date: time to address the identity crisis**

*Barbara sustained a lumbar vertebral fracture aged 76 and was referred for a fracture and falls risk assessment. Her bone mineral density (BMD) was above the World Health Organisation (WHO) cut-off for diagnosing osteoporosis, and she was informed she did not have osteoporosis. In line with international guidance however, a drug treatment for osteoporosis was recommended. She decided not to take it.*

Osteoporosis is a systemic skeletal disease characterised by low bone mass and microarchitectural deterioration of bone tissue, with a consequent increase in bone fragility and susceptibility to fracture. [1] In recent years, an ‘osteoporosis crisis’ has been described, characterised by poor treatment uptake and the consequent high levels of preventable fracture. [2] We suggest that a significantly overlooked influence on poor treatment uptake is the *international inconsistency* regarding how the diagnostic label of osteoporosis is applied, and that it is timely for this to be reviewed.

Since 1994, the operational definition of osteoporosis, defined by the World Health Organisation, has been based on the T-score for BMD assessed at the femoral neck, defined as a value for BMD 2.5 SD or more below the young female adult mean (T-score ≤−2.5 SD). [1] BMD that lies between 2.5 and 1 SD below the young female adult mean is classified as osteopenic. These diagnostic thresholds were welcomed as an important advance for clinical management. However, in the last 15 years, there has been a step-change in the field of osteoporosis, namely to base osteoporosis management not just on absolute values of bone mineral density (BMD), but on broader consideration of future fracture risk.[3] This change has been underpinned by observations that the majority of patients with a fragility fracture do not have osteoporotic BMD [4], that aggregates of risk factors (calculated using algorithms such as FRAX), perform better than BMD alone in predicting those at risk of subsequent fracture,[3] and that osteoporosis treatments have proven efficacy in reducing fracture risk in patients with non-osteoporotic levels of BMD.[5] Despite the well-accepted notion that treatment decisions should be informed by factors other than/in addition to BMD (e.g. prior fractures and calculated fracture risk), the WHO diagnosis, endorsed by current UK and European guidance, [3,6] still relies purely on BMD testing. This means the diagnosis no longer relates to the population for whom osteoporosis drugs are recommended, i.e. the population known to have bone fragility and susceptibility to fracture.

In our view, inconsistency about the application of the osteoporosis label causes confusion for clinicians and patients like Barbara for a number of reasons.

First, many patients who fracture easily and are recommended osteoporosis drugs, do not receive a diagnosis of osteoporosis. This may be because they do not have a BMD assessment (DXA scan); in the UK, treatment is recommended without need for a DXA in patients aged 75 and over. Alternatively, patients may not receive a diagnosis of osteoporosis because their BMD is spuriously raised, e.g. in the presence of osteoarthritis; or, their BMD is within the osteopenic range. From a sociological perspective, receiving a diagnosis or label is an important first step in making sense of, and accepting a condition. [7,8]Qualitative research has demonstrated that the absence of a diagnosis of osteoporosis results in difficulty making sense of the need for osteoporosis medicines. [9]

Second, a diagnosis of osteoporosis based purely on BMD can result in patients being ‘cured’ of their condition. However, osteoporosis is a chronic condition, and treated osteoporosis is still osteoporosis. [10] Third, interpretation of the BMD Z-score result, which defines BMD in SDs above or below an aged-matched mean, may lead to patients being informed their bone density is osteoporotic, but normal for age. This reinforces the notion of a condition which is synonymous with age and which has inevitable consequences, suggesting that pharmaceutical intervention may be futile. [11]

Current levels of adherence with bisphosphonate therapy are known to be poor. [12] Multiple qualitative studies identify that poor adherence is associated with health beliefs such as perceiving osteoporosis as normal for age, not understanding what osteoporosis is or what treatment is for, and confusion about BMD results. [9,11]

At least two alternative diagnostic approaches have been proposed. In the UK, the 2018/19 General Medical Services Quality and Outcomes Framework (QOF) states that in those aged 75 and over with fragility fractures, a clinical diagnosis of osteoporosis can be assumed [13]. In 2014, the National Bone Health Alliance (NBHA) Working Group proposed that the diagnosis of osteoporosis should be widened even further, to include postmenopausal women and men aged 50 and over with hip fractures, with other low trauma fractures in the presence of osteopenia, and in those with high fracture risk calculated using FRAX, in addition to those meeting the WHO definition. [14]

Ensrud et al evaluated the effect of the NHBA and a more clinical definition (defined as those aged 80 and over with BMD meeting the WHO definition *plus* those with incident hip- or prevalent vertebral fracture) [15] thresholds on probability of hip fracture. They demonstrated that the NHBA diagnosis resulted in the doubling of the proportion of women identified as treatment candidates. [15]. However, using their own clinical definition, women, who already met criteria for treatment, had a higher 5-year probability of hip fracture, despite accounting for competing mortality risk, than women with ‘high fracture risk’. [15] So, available evidence indicates that including a clinical component to the diagnosis as Ensrud and colleagues suggests will not change the population eligible and targeted for evidence-based intervention (avoiding concerns about over-treatment) and performs well at predicting those most in need of treatment.

We believe it is time for the World Health Organisation and the International Society for Clinical Densitometry to consider a broader definition of osteoporosis which encompasses a clinical diagnosis, and, to provide clear guidance on communicating BMD results to patients. A consistent international approach is essential to reduce confusion among clinicians and patients and promote treatment adherence in those at elevated risk of future fracture.

References

1. Kanis JA, Melton III LJ, Christiansen C, Johnston CC, Khaltaev N. The diagnosis of osteoporosis*. Journal of bone and mineral research*. 1994;9(8):1137-1141.

2. Khosla, S, Shane, E. A crisis in the treatment of osteoporosis. *Journal of Bone and Mineral Research* 2016; 31(8): 1485-1487.

3. Kanis JA, Cooper C, Rizzoli R, Reginster J-, on behalf of the Scientific Advisory Board of the European Society for Clinical and Economic Aspects of Osteoporosis (ESCEO) and the Committees of Scientific Advisors and National Societies of the International Osteoporosis Foundation. European guidance for the diagnosis and management of osteoporosis in post-menopausal women. Osteoporos Int. 2019;30(1):3-44.

4. Siris ES, Chen YT, Abbott TA, Barrett-Connor E, Miller PD, Wehren LE, Berger ML. Bone mineral density thresholds for pharmacological intervention to prevent fractures. Archives of internal medicine. 2004 May 24;164(10):1108-12.

5. Reid IR, Horne AM, Mihov B, et al. Fracture prevention with zoledronate in older women with osteopenia*. N Engl J Med*. 2018;379(25):2407-2416.

6. Compston J, Cooper A, Cooper C, Gittoes N, Gregson C, Harvey N, Hope S, Kanis JA, McCloskey EV, Poole KE, Reid DM. UK clinical guideline for the prevention and treatment of osteoporosis. Archives of osteoporosis. 2017 Dec 1;12(1):43.

7. Brown, P., 1995. Naming and framing: the social construction of diagnosis and illness. *Journal of health and social behavior*, pp.34-52.

8. Hale ED, Treharne GJ, Kitas GD. The Common-Sense Model of self-regulation of health and illness: how can we use it to understand and respond to our patients’ needs?. Rheumatology. 2007 Jun 1;46(6):904-6.

9. Salter, C.I., Howe, A., McDaid, L., Blacklock, J., Lenaghan, E. and Shepstone, L., 2011. Risk, significance and biomedicalisation of a new population: Older women’s experience of osteoporosis screening. *Social Science & Medicine*, *73*(6), pp.808-815.

10. Lewiecki EM, Binkley N, Bilezikian JP. Treated Osteoporosis Is Still Osteoporosis. Journal of Bone and Mineral Research. 2019 Apr;34(4):605-6.

11. Raybould, G., Babatunde, O., Evans, E., Jordan, J.L., Paskins Z. Expressed information needs of patients with osteoporosis and/or fragility fractures: a qualitative systematic review*.* Arch Osteoporos (2018) 13: 55.

12. Siris ES, Harris ST, Rosen CJ, Barr CE, Arvesen JN, Abbott TA, Silverman S. Adherence to bisphosphonate therapy and fracture rates in osteoporotic women: relationship to vertebral and nonvertebral fractures from 2 US claims databases. Mayo Clinic Proceedings 2006 Aug 1 (Vol. 81, No. 8, pp. 1013-1022).

13. NHS England. 2018/19 General Medical Services (GMS) contract Quality and Outcomes Framework (QOF)Guidance for GMS contract 2018/19 Available at https://www.nhsemployers.org/-/media/Employers/Documents/Primary-care-contracts/QOF/2018-19/2018-19-QOF-guidance-for-stakeholders.PDF

14. Siris ES, Adler R, Bilezikian J, Bolognese M, Dawson-Hughes B, Favus MJ, Harris ST, De Beur SJ, Khosla S, Lane NE, Lindsay R. The clinical diagnosis of osteoporosis: a position statement from the National Bone Health Alliance Working Group. Osteoporosis international. 2014 May 1;25(5):1439-43.

15. Ensrud, K.E., Kats, A.M., Boyd, C.M., Diem, S.J., Schousboe, J.T., Taylor, B.C., Bauer, D.C., Stone, K.L. and Langsetmo, L., 2019. Association of disease definition, comorbidity burden, and prognosis with hip fracture probability among late-life women. *JAMA internal medicine*.2019: doi:10.1001/jamainternmed.2019.0682