



Intervention thresholds and diagnostic thresholds in the management of osteoporosis

John A. Kanis^{1,2} · Eugene V. McCloskey^{1,3} · Nicholas C. Harvey^{4,5} · Cyrus Cooper^{4,5,6} · Rene Rizzoli⁷ · Bess Dawson-Hughes⁸ · Stefania Maggi⁹ · Jean-Yves Reginster^{10,11}

Received: 11 July 2022 / Accepted: 29 July 2022 / Published online: 7 November 2022
© The Author(s) 2022

Keywords Osteoporosis · Definition · Intervention thresholds · FRAX · Fracture risk · Diagnosis

Following calls to change the definition of osteoporosis [1, 2], a position paper of the International Osteoporosis Foundation (IOF) and the European Society for Clinical and Economic Aspects of Osteoporosis, Osteoarthritis and Musculoskeletal Diseases (ESCEO) recently addressed the rationale for separate diagnostic and intervention thresholds in osteoporosis [3]. The conclusions of the working group are given below.

The low rate of treatment in patients who have sustained a fragility fracture appears to underlie the calls for a change in the diagnostic criteria for osteoporosis, but there is little evidence that this alone would improve management in such patients. The WHO BMD-based, operational definition of osteoporosis is analogous to that employed successfully for the use of continuously distributed clinical risk variables in the management and prevention of other multifactorial outcomes, such as myocardial infarction (by defining hypercholesterolaemia) and stroke (by defining hypertension). It

has yielded a regulatory framework in the USA, EU and elsewhere which has permitted the development of an enviable armamentarium of therapeutic interventions.

The confusion appears to arise because of the erroneous conflation of diagnostic and intervention thresholds. The example used for the basis of the paper by Paskins and colleagues [2] illustrates this clearly, namely a 76-year-old woman with a recent vertebral fracture. Here, the diagnosis is one of fragility fracture, which like a diagnosis of myocardial infarction or stroke, should initiate a course of interventions, including pharmacological agents, to reduce future risk of recurrence. The need for a parallel diagnosis of BMD-defined osteoporosis serves to delay and indeed limit access to treatment, particularly where the result is misinterpreted, possibly fuelled by the previous misconceptions that the treatments do not work in the absence of BMD-defined osteoporosis [4, 5]. Importantly, there is increasing evidence that the implementation of fracture liaison services though

✉ John A. Kanis
w.j.pontefract@sheff.ac.uk

¹ Centre for Metabolic Bone Diseases, University of Sheffield Medical School, Beech Hill Road, Sheffield S10 2RX, UK

² Mary McKillop Institute for Health Research, Australian Catholic University, Melbourne, Australia

³ Centre for Integrated Research in Musculoskeletal Ageing (CIMA), Mellanby Centre for Musculoskeletal Research, University of Sheffield, Sheffield, UK

⁴ MRC Lifecourse Epidemiology Centre, University of Southampton, Southampton SO16 6YD, UK

⁵ NIHR Southampton Biomedical Research Centre, University of Southampton and University Hospital Southampton NHS Foundation Trust, Tremona Road, Southampton, UK

⁶ NIHR Oxford Biomedical Research Centre, University of Oxford, Oxford, UK

⁷ Service of Bone Diseases, Geneva University Hospitals and Faculty of Medicine, 1211 Geneva 14, Switzerland

⁸ Jean Mayer USDA Human Nutrition Research Center on Aging, Tufts University, Boston, MA, USA

⁹ Institute of Neuroscience, Aging Branch, CNR, Padua, Italy

¹⁰ WHO Collaborating Center for Epidemiology of Musculoskeletal Health and Aging, Liège, Belgium

¹¹ Division of Public Health, Epidemiology and Health Economics, University of Liège, CHU Sart Tilman B23, 4000 Liège, Belgium

campaigns, such as Capture the Fracture can improve access to better management and treatment leading to reductions in future fractures [6].

It is widely recognised that BMD alone for fracture risk assessment is less sensitive than risk assessment algorithms, such as FRAX® that incorporate risk indicators in addition to BMD [7]. It is certainly relevant to question the need for diagnostic criteria when the field is moving towards risk-based assessment and intervention, including adjustments to FRAX and guidance thresholds to distinguish high risk from very high risk to optimise the use of anabolic agents [8–12]. These developments will inevitably decrease the clinical utility of the T-score, but they will, however, take time to implement into routine clinical practice. Notwithstanding, the current diagnostic criteria will remain of value in quantifying the burden of disease and the development of strategies to combat osteoporosis in the foreseeable future.

It is hard to argue that operational BMD-based definition is anything other than a triumph in healthcare, and there appears little possible (or indeed intellectually sound) reason to argue for a change. Those suggesting an alteration to the diagnostic criteria for osteoporosis would do well to consider the implications of such an approach if it were to be adopted more widely. Would they really be happy with diagnosing hypertension purely on the basis of a stroke or myocardial infarction? In our view, the proposal is intellectually constrained, inadequately justified and may well inappropriately reflect the pressures of reimbursement led healthcare.

We recommend that the BMD-based definition of osteoporosis be retained whilst further clarity is brought to bear on the distinction between BMD-based diagnoses and intervention thresholds.

Declarations

Conflict of interest JA Kanis led the team that developed FRAX. EV McCloskey has received consultancy/lecture fees/Grant funding/honoraria from AgNovos, Amgen, AstraZeneca, Consilient Healthcare, Fresenius Kabi, Gilead, GSK, Hologic, Internis, Lilly, Merck, Novartis, Pfizer, Radius Health, Redx Oncology, Roche, SanofiAventis, Servier, Synexus, UCB, Viiv, Warner Chilcott, I3 Innovus and Unilever. NC Harvey reports personal fees, consultancy, lecture fees and honoraria from Alliance for Better Bone Health, AMGEN, MSD, Eli Lilly, UCB, Kyowa Kirin, Servier, Shire, Consilient Healthcare and Internis Pharma, outside the submitted work. C Cooper reports personal fees from Alliance for Better Bone Health, Amgen, Eli Lilly, GSK, Medtronic, Merck, Novartis, Pfizer, Roche, Servier, Takeda and UCB. R Rizzoli has received fees for lectures or advisory boards from Abiogen, Amgen, Danone, Echolight, European Milk Forum, Mithra, Nestlé, ObsEva, Pfizer Consumer Health, Radius Health, Rejuvenate and Theramex, outside the submitted work. B

Dawson-Hughes is on the Data Safety Monitoring Board of AgNovos, outside the submitted work. S Maggi reports grants from Sanofi, MSD, GSK, Pfizer, Takeda, Mylan through institution as organizer of meetings/congresses and as principal investigator of epidemiological studies, for taking part to advisory boards and expert meetings. J-Y Reginster has received fees for lectures or advisory boards from IBSA-Genevriev, Mylan, Radius Health, Pierre Fabre, Faes Pharma, Rejuvenate Biomed, Teva, Theramex, Pfizer, Mithra Pharmaceuticals, CNIEL, Dairy Research Council, Nutricia, Danone and Agnovos, and industry grants (all through institution) from IBSA-Genevriev, Mylan, CNIEL, Radius Health and TRB, outside the submitted work.

Statement of human and animal rights This study does not contain any studies with human participants or animals performed by any of the authors.

Informed consent For this type of article, formal consent is not relevant or required.

Open Access This article is licensed under a Creative Commons Attribution 4.0 International License, which permits use, sharing, adaptation, distribution and reproduction in any medium or format, as long as you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons licence, and indicate if changes were made. The images or other third party material in this article are included in the article's Creative Commons licence, unless indicated otherwise in a credit line to the material. If material is not included in the article's Creative Commons licence and your intended use is not permitted by statutory regulation or exceeds the permitted use, you will need to obtain permission directly from the copyright holder. To view a copy of this licence, visit <http://creativecommons.org/licenses/by/4.0/>.

References

1. Siris ES, Adler R, Bilezikian J et al (2014) The clinical diagnosis of osteoporosis: a position statement from the National Bone Health Alliance Working Group. *Osteoporos Int* 25:1439–1443
2. Paskins Z, Ong T, Armstrong DJ (2020) Bringing osteoporosis up to date: time to address the identity crisis. *Age Ageing* 49:329–331
3. Kanis JA, McCloskey EV, Harvey NC et al (2022) The need to distinguish intervention thresholds and diagnostic thresholds in the management of osteoporosis. *Osteoporos Int*. <https://doi.org/10.1007/s00198-022-06567-9>
4. Kanis JA, McCloskey E, Johansson H et al (2012) FRAX® with and without bone mineral density. *Calcif Tiss Int* 90:1–13
5. McCloskey E (2016) A BMD threshold for treatment efficacy in osteoporosis? A need to consider the whole evidence base. *Osteoporos Int* 27:417–419
6. Javaid MK, Kyer C, Mitchell PJ et al (2015) Effective secondary fracture prevention: implementation of a global benchmarking of clinical quality using the IOF Capture the Fracture(R) Best Practice Framework tool. *Osteoporos Int* 26:2573–2578
7. Kanis JA, Harvey NC, Johansson H et al (2020) A decade of FRAX: how has it changed the management of osteoporosis? *Aging Clin Exp Res* 32:187–196
8. Kanis JA, Harvey NC, McCloskey E et al (2020) Algorithm for the management of patients at low, high and very high risk of osteoporotic fracture. *Osteoporos Int* 31:1–12
9. Kanis JA, Johansson H, Harvey NC et al (2021) An assessment of intervention thresholds for very high risk applied to the NOGG guidelines. A report for the National Osteoporosis Guideline Group (NOGG). *Osteoporos Int* 32:1951–1960

10. McClung MR (2021) Role of bone-forming agents in the management of osteoporosis. *Aging Clin Exp Res* 33:775–791
11. Curtis EM, Reginster JY, Al-Daghri N et al (2022) Management of patients at very high risk of osteoporotic fractures through sequential treatments. *Aging Clin Exp Res* 34:695–714
12. Camacho PM, Petak SM, Binkley N et al (2020) American Association of Clinical Endocrinologists/American College of Endocrinology clinical practice guidelines for the diagnosis and treatment of postmenopausal osteoporosis-2020 update. *Endocr Pract* 26:1–46

Publisher's Note Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.