



Screening for high fracture risk

E. McCloskey^{1,2,3} · N. Harvey^{4,5} · H. Johansson^{1,6} · M. Lorentzon^{6,7,8} · L. Vandenput^{6,9} · J.A. Kanis^{1,6}

Received: 3 March 2020 / Accepted: 8 April 2020 / Published online: 24 April 2020
© International Osteoporosis Foundation and National Osteoporosis Foundation 2020

Sir,

The conclusion by Merlijn and colleagues that consideration should be given to the implementation of population screening for high fracture risk is welcome [1]. However, their meta-analysis is limited by its lack of critique of the studies included, particularly when objective criteria for population-based screening are applied.

Key principles for a successful screening programme were first proposed by the WHO over 50 years ago [2]. These criteria, slightly modified, are still of importance today [3]. In contrast to the SCOOP and ROSE studies [4, 5], the SOS study does not meet many of these key requirements [6]. Notably, the screening test should be simple, safe, precise and validated. In contrast to SCOOP and ROSE, where the FRAX questionnaire was followed by BMD in a subset to either generate an updated FRAX score including BMD (SCOOP) or a simple T-score intervention threshold (ROSE), in the SOS study, it is very difficult to determine exactly how the high-risk group was constituted [6].

For SOS, screening consisted of dual energy X-ray absorptiometry (DXA), vertebral fracture assessment (VFA), risk factor evaluation for fractures (FRAX), falls and blood tests to exclude secondary osteoporosis [6]; this essentially represents an attempt at full clinical assessment rather than a simplified screening test. Furthermore, it is impossible to derive the contribution of each of these tests to subsequent inclusion

in the ‘high-risk’ group for treatment. How many were treated solely on the basis of FRAX major osteoporotic fracture probability above age-dependent thresholds in combination with a DXA T-score ≤ -2 ? How many were treated based on the current Dutch primary care guidelines (vertebral fracture and/or a BMD T-score ≤ -2.5) [7]? Indeed, what were the criteria for vertebral fracture definition on VFA, and who conducted this assessment? The false positive rate for such fractures is well recognised [8, 9]. Finally, the consideration of falls in the decision-making process is not described.

The criteria for a screening programme also state that for any test a suitable cutoff level should be defined and agreed for further investigation and/or treatment. The complex nature of the differing pathways and thresholds for treatment in SOS, and the final advice about treatment (‘personalized treatment advice, formulated by an expert team of experienced GPs’) made it difficult to ensure that the treatment group was actually at high risk of fracture. Surprisingly, those recommended for treatment were of similar age or slightly younger than those not recommended for treatment. They did not differ in the prevalence of any risk factors apart from prior fracture and family history of fracture (both only approximately 30–34% higher in the treated group), but with lower rates of poor mobility and walking aid use (both 30–33% lower) [6]. This reinforces the view that the screening methodology was wanting, and illustrates that the SOS study was not actually in

✉ E. McCloskey
e.v.mccloskey@sheffield.ac.uk

¹ Centre for Metabolic Bone Diseases, University of Sheffield, Sheffield, UK

² Centre for Integrated research in Musculoskeletal Ageing (CIMA), Mellanby Centre for Bone Research, University of Sheffield, Sheffield, UK

³ Metabolic Bone Centre, Northern General Hospital, Herries Road, Sheffield S5 7AU, UK

⁴ MRC Lifecourse Epidemiology Unit, University of Southampton, Southampton, UK

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

⁶ Mary McKillop Institute for Health Research, Australian Catholic University, Melbourne, Australia

⁷ Geriatric Medicine, Department of Internal Medicine and Clinical Nutrition, Institute of Medicine, University of Gothenburg, Gothenburg, Sweden

⁸ Region Västra Götaland, Geriatric Medicine, Sahlgrenska University Hospital, Mölndal, Sweden

⁹ Centre of Bone and Arthritis Research, Department of Internal Medicine and Clinical Nutrition, Institute of Medicine, Sahlgrenska Academy, University of Gothenburg, Gothenburg, Sweden

keeping with the title of the systematic review. This poor case selection is markedly different from the high-risk group identified in the SCOOP study, where all the risk factors including falls were over-represented in the high-risk group with 2–4-fold greater frequency of prior fracture or parental hip fracture compared with the control group [4].

The important caveats described above, and other shortcomings of the SOS study including low participation, medication uptake and adherence [6, 10], are important as the authors have oddly decided to undertake a sensitivity analysis that excluded the SCOOP trial [1]. We strongly suggest that a much more appropriate sensitivity analysis would be to omit SOS, and we invite the authors to undertake this investigation. The unquestioned inclusion of SOS in the meta-analysis has the real risk of underestimating the effects of screening programmes, particularly those more appropriately based on fracture risk, and thus has the potential to hinder their implementation.

Compliance with ethical standards

Conflict of interest Eugene McCloskey Nicholas Harvey, Helena Johansson, Mattias Lorentzon, Liesbeth Vandenput and John A Kanis declare that they have no conflict of interest.

References

1. Merlijn T, Swart KMA, van der Horst HE, Netelenbos JC, Elders PJM (2020) Fracture prevention by screening for high fracture risk: a systematic review and meta-analysis. *Osteoporos Int* 31:251–257
2. Wilson JMG, Jungner G (1968) Principles and practice of screening for disease. World Health Organization <https://apps.who.int/iris/handle/10665/37650>,
3. UK National Screening Committee (2015) Criteria for appraising the viability, effectiveness and appropriateness of a screening programme (<https://www.gov.uk/government/publications/evidence-review-criteria-national-screening-programmes/criteria-for-appraising-the-viability-effectiveness-and-appropriateness-of-a-screening-programme>)
4. Shepstone L, Lenaghan E, Cooper C, Clarke S, Fong-Soe-Khioe R, Fordham R, Gittoes N, Harvey I, Harvey N, Heawood A, Holland R, Howe A, Kanis J, Marshall T, O'Neill T, Peters T, Redmond N, Torgerson D, Turner D, McCloskey E, Shepstone L, Lenaghan E, Cooper C, Clarke S, Fong-Soe-Khioe R, Fordham R, Gittoes N, Harvey I, Harvey N, Heawood A, Holland R, Howe A, Kanis J, Marshall T, O'Neill T, Peters T, Redmond N, Torgerson D, Turner D, McCloskey E, Crabtree N, Duffy H, Parle J, Rashid F, Stant K, Taylor K, Thomas C, Knox E, Tenneson C, Williams H, Adams D, Bion V, Blacklock J, Dyer T, Bratherton S, Fidler M, Knight K, McGurk C, Smith K, Young S, Collins K, Cushnaghan J, Arundel C, Bell K, Clark L, Collins S, Gardner S, Mitchell N (2018) Screening in the community to reduce fractures in older women (SCOOP): a randomised controlled trial. *Lancet* 391:741–747
5. Rubin KH, Rothmann MJ, Holmberg T, Høiberg M, Möller S, Barkmann R, Glüer CC, Hermann AP, Bech M, Gram J, Brixen K (2018) Effectiveness of a two-step population-based osteoporosis screening program using FRAX: the randomized Risk-stratified Osteoporosis Strategy Evaluation (ROSE) study. *Osteoporos Int* 29:567–578
6. Merlijn T, Swart KM, van Schoor NM et al (2019) The effect of a screening and treatment program for the prevention of fractures in older women: a randomized pragmatic trial. *J Bone Miner Res* 34: 1993–2000
7. Elders PJM, Dinant GJ, Van Geel T, Maartens LWF, Merlijn T, Geijer RMM, Geraets JJXR (2012) NHG-Standaard Fractuurpreventie (Tweede herziening). *Huisarts Wet* 55:452–458
8. Jiang G, Eastell R, Barrington NA, Ferrar L (2004) Comparison of methods for the visual identification of prevalent vertebral fracture in osteoporosis. *Osteoporos Int* 15:887–896
9. Ferrar L, Jiang G, Schousboe JT, DeBold CR, Eastell R (2008) Algorithm-based qualitative and semiquantitative identification of prevalent vertebral fracture: agreement between different readers, imaging modalities, and diagnostic approaches. *J Bone Miner Res* 23:417–424
10. Kanis JA, Harvey NC, Johansson H, Liu E, Vandenput L, Lorentzon M, Leslie WD, McCloskey EV (2020) A decade of FRAX: how has it changed the management of osteoporosis? *Aging Clin Exp Res* 32:187–196

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