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OVERDIAGNOSING BONE FRAGILITY

Authors’ reply to Lee and colleagues

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Lee and colleagues of the National Bone Health Alliance (NBHA) call for expanded fracture liaison services (FLS), because secondary prevention represents the most productive opportunity for pharmacotherapy. Intuitively this seems logical, but supporting arguments do not stand up to scrutiny.1 2

The effectiveness of FLS should be tested in randomised controlled trials (RCTs) to see whether this approach can achieve the “quality outcomes” referred to—prevention of second fractures—as opposed to the proportion of patients evaluated or prescribed drugs. Presently, evidence on FLS is limited to observational studies or invalid modelling based cost effectiveness extrapolations.3

Lee and colleagues cite HORIZON—the only secondary prevention trial of patients after a hip fracture—as proof that FLS are effective.4 However, after median follow-up of nearly two years, secondary hip fracture rates did not differ significantly with zoledronic acid versus placebo (2.0% v 3.5%). There were fewer clinical non-vertebral fractures (7.6% v 10.7%; absolute risk reduction 3.1%; relative risk reduction 27%; P=0.03) and fewer clinical vertebral fractures (1.7% v 3.8%; 2.1% v 55%; P=0.02). But even under “artificial” circumstances for assessing effectiveness,5 patients did not benefit from pharmacotherapy. Fundamental flaws including early termination, selective outcome reporting, and loss to follow-up undermine HORIZON’s generalisability. Moreover, participants’ mean age was only 74 years, whereas the mean age of patients with hip fracture is about 80 years in Europe, and more than three in four hip fractures occur in people over 75.

We share NBHA’s desire to prevent clinically important fractures. Nonetheless, we must abstain from interventions (a) that are not proved effective, (b) for which the ratio of potential benefit to potential harm is poor, or (c) for which cost prohibits the development of more effective alternative strategies. Pending demonstration of the utility of FLS in a valid RCT, we recommend discretion in advocating and implementing this concept.

Vigorous discussion of current scientific evidence on how best to reduce fracture burden is important. Orthodoxy, inattention to methodological problems in RCTs, and lack of transparency concerning competing interests remain barriers to achieving the best and most cost effective care for our patients.6

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