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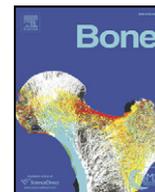
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Reply to Letter to the Editor

Modelling cost-effectiveness in osteoporosis

We thank Dr. Stevenson for raising several important issues. Matt Stevenson, who developed the model used by the National Institute for Health and Clinical Excellence (NICE), is correct in stating that the model he used took account of deaths occurring after 10 years. The limitations of using a 10-year time horizon were illustrated using death by way of an example. Whereas deaths after 10 years were 'bolted' onto the NICE model, none of the other consequences of fracture was included. Our own sensitivity analyses and previous observations [1] attest to a very large effect of restricting the time horizon. It is important, therefore, to determine the sensitivity of the NICE model to changes in the time horizon.

That apart, there are other differences in the construct of the NICE model that impact on cost-effectiveness. The NICE model claimed to follow the construct recommended by the World Health Organization (WHO) [2,3] but differed in several important respects. First, it used body mass index as a dichotomous rather than a continuous variable, thereby devaluing its utility. Second, several risk factors were omitted (glucocorticoids is an important example) or the threshold changed (alcohol intake) without regard to the manner in which these changes affected the β coefficients. Third, no account was taken of the effects of the clinical risk factors on the death hazard. Notwithstanding Dr. Stevenson's assertion that he obtains similar results if he uses our assumptions in the NICE model, in the absence of explicit numerical data to support his statement it cannot be assumed that the differences lie predominantly in the assumptions used.

These considerations apart, there are differences in the assumptions used to populate the model. Most of these were modelled in sensitivity analyses [4]. For example, the inclusion of side effects of alendronate had a very small impact on cost-effectiveness using the assumptions in the report commissioned by NICE. It was only when these were multiplied 10-fold for reasons that are difficult to understand, that a significant adverse effect on cost-effectiveness was evident. With regard to the efficacy of alendronate, we preferred to use Dr. Stevenson's own meta-analysis [5], rather than that derived by NICE using data for some (but not all) bisphosphonates.

A major point of difference in the assumptions used by NICE and us lies in the cost for the identification of patients at risk. Imagine, for example that 1% of women aged 50 years might have a fracture probability that exceeded an intervention threshold, then 100 BMD tests would be required to identify one patient for treatment at this age; this in turn has a marked adverse impact on cost-effectiveness by building in the cost of screening individuals who would not be treated. We have not favoured this approach since neither we nor many authoritative bodies (e.g. Royal College of Physicians, Bone Research Society, the EU, WHO, the European Society for Clinical and Economic Aspects of Osteoporosis and Osteoarthritis or the International Osteoporosis Foundation) advocate mass population

based screening [3,6–11]. The evidence base for population screening is just not there. Whether improved methods of case finding might lend themselves to screening requires to be tested, and large trials to address this are currently underway in the UK, funded by the Medical Research Council and Arthritis and Rheumatism Council. For these reasons, we followed the practice currently adopted by the Royal College of Physicians and that used in many countries of an opportunistic case finding strategy where patients are considered for BMD testing in the presence of 1 or more clinical risk factors.

Under the current guidance of the Royal College of Physicians, those with a prior fracture are eligible for treatment without BMD testing (a strategy shown to be cost-effective in our analysis). There is, therefore, no requirement for BMD testing in this group of patients. In women with other risk factors, BMD testing should be undertaken for those in whom the probability of reclassification (high to low risk, or low to high risk) is high. Women who qualify for a BMD assessment in this way do not outnumber those with a prior fracture (using assessment thresholds currently being developed for the UK). Thus the requirement for BMD testing does not exceed 1/patient identified – exactly that which we modelled in our paper.

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