**Bisphosphonates in osteoporosis: NICE and easy?**

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The recent National Institute for Health and Care Excellence (NICE) updated Multiple Technology Appraisal (MTA) on bisphosphonate use in osteoporosis1 demonstrates how, for a common disorder, the strict application of cost-effectiveness thresholds for relatively inexpensive drugs may lead to counter-intuitive and potentially harmful guidance2. The MTA incorporates the development of fracture risk calculators based on individualized clinical risk factors, such as FRAX and QFracture, (recommended by NICE for the assessment of fracture risk in certain sections of the population3), and also the widespread availability of low-cost generic forms of the main oral and intravenous bisphosphonates. This latter development has led, in the NICE analysis, to cost-effectiveness at very low risk thresholds, resulting in an appraisal which recommends that, amongst individuals who qualify for osteoporosis assessment on the basis of NICE Clinical Guideline CG1463, treatment with oral bisphosphonates may be instituted above a 1% probability of major osteoporotic fracture (hip, spine, wrist or humerus) over 10 years, or above 10% for intravenous bisphosphonates. These health-economic-derived thresholds create a real danger of excessive bisphosphonate prescription in the general population2, with treatment of substantial numbers of people who are at very low individual fracture risk; for example, every person eligible for assessment under CG146, including all women aged ≥65 and men ≥75 years, would be recommended treatment if the MTA recommendations were interpreted as intervention thresholds4. Very rare, but serious, side-effects of bisphosphonate treatment, such as atypical femur fracture and osteonecrosis of the jaw, would be observed far more commonly in the population than at present. Furthermore, the risk/benefit balance for individuals at low risk would be adversely affected, in contrast to the very clearly positive benefit/risk ratio associated with intervention at more clinically appropriate treatment thresholds4-6.

Whilst the NICE document makes reference to the approach to assessment and intervention thresholds established by the UK National Osteoporosis Guideline Group (NOGG, recently NICE-accredited)4, this appears outwith the recommendations, and states incorrectly that the NOGG thresholds have not been shown to be cost-effective. Indeed, the intervention thresholds of NOGG are higher at all ages than those deemed cost-effective in the current MTA7. Whilst the derivation of treatment thresholds is necessarily arbitrary, NOGG developed its guidance on the basis of clinical appropriateness, setting the threshold at the age-specific probability of fracture equivalent to women having already sustained a fracture. Thus, economic thresholds were not used to set intervention thresholds but, more appropriately, to validate the use of clinically driven intervention thresholds. This approach, which avoids inappropriate over-treatment of older individuals and under-treatment of younger individuals, has indeed been shown to be cost-effective8, and has been adopted in many countries9.

In conclusion, unthinking assimilation of the NICE MTA risks a generation of older individuals taking a bisphosphonate, regardless of benefit/risk balance at the individual level, and a resulting increased burden of rare long-term side-effects across the population. Given recent debates about the role of pharmaceutical interventions in the prevention of several chronic non-communicable diseases10, this would be an unexpected, and entirely unwelcome, consequence of national guidance.

**Declaration of interests**

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**Authorship statement**

All authors contributed to the initial drafting, revision and finalization of the manuscript. All authors approved the final submitted manuscript.

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